UC-NRLF
B 3 135 916

EXCHANGE

SIGILLVM · VNIVERSITATIS · CALIFORNIENSIS
FIAT LVX
MDCCCLXVIII

EX LIBRIS

BIOLOGY
LIBRARY
G

EXCHANGE
JUL 20 1920

Physiological Studies

(First Series)

By

J. A. MacWilliam, M.D., F.R.S.
Professor of Physiology

J. E. Kesson, M.D.

G. Spencer Melvin, M.D.

James R. Murray, M.D.

Edward S. Edie, M.A., B.Sc.

LIBRARY
OF THE
UNIVERSITY
OF
CALIFORNIA

Printed for the University of Aberdeen
1916

Aberdeen University
Studies : No. 72

Physiological Studies

(First Series)

University of Aberdeen.

COMMITTEE ON PUBLICATIONS.

Convener: Professor JAMES W. H. TRAIL, F.R.S., Curator of the Library.

General Editor: P. J. ANDERSON, LL.B., Librarian to the University.

1900. No. 1.—*Roll of Alumni in Arts of King's College*, 1596-1860. P. J. Anderson.
„ No. 2.—*Records of Old Aberdeen*, 1157-1891. A. M. Munro, F.S.A. Scot. Vol. I.
„ No. 3.—*Place Names of West Aberdeenshire.* James Macdonald, F.S.A. Scot.
1901. No. 4.—*Family of Burnett of Leys.* George Burnett, LL.D., Lyon King of Arms.
„ No. 5.—*Records of Invercauld*, 1547-1828. Rev. J. G. Michie, M.A.
1902. No. 6.—*Rectorial Addresses in the Universities of Aberdeen*, 1835-1900. P. J. Anderson.
„ No. 7.—*Albemarle Papers*, 1746-48. Professor C. S. Terry, M.A.
1903. No. 8.—*House of Gordon.* J. M. Bulloch, M.A. Vol. I.
„ No. 9.—*Records of Elgin.* William Cramond, LL.D. Vol. I.
1904. No. 10.—*Avogadro and Dalton.* A. N. Meldrum, D.Sc.
„ No. 11.—*Records of the Sheriff Court of Aberdeenshire.* David Littlejohn, LL.D. Vol. I.
„ No. 12.—*Proceedings of the Anatomical and Anthropological Society*, 1902-04.
1905. No. 13.—*Report on Alcyonaria.* Professor J. Arthur Thomson, M.A., and others.
„ No. 14.—*Researches in Organic Chemistry.* Prof. F. R. Japp, F.R.S., and others.
„ No. 15.—*Meminisse Juvat: with Appendix of Alakeia.* Alexander Shewan, M.A.
„ No. 16.—*Blackhalls of that Ilk and Barra.* Alexander Morison, M.D.
1906. No. 17.—*Records of the Scots Colleges.* Vol. I. P. J. Anderson.
„ No. 18.—*Roll of the Graduates*, 1860-1900. Colonel William Johnston, C.B., M.D., LL.D.
„ No. 19.—*Studies in the History of the University.* P. J. Anderson and others.
„ No. 20.—*Studies in the History and Art of the Eastern Provinces of the Roman Empire.* Professor Sir W. M. Ramsay, D.C.L., and pupils.
„ No. 21.—*Studies in Pathology.* William Bulloch, M.D., and others.
„ No. 22.—*Proceedings of the Anatomical and Anthropological Society*, 1904-06.
„ No. 23.—*Subject Catalogues of the Science Library and the Law Library.* P. J. Anderson.
„ No. 24.—*Records of the Sheriff Court of Aberdeenshire.* David Littlejohn, LL.D. Vol. II.
1907. No. 25.—*Studies on Alcyonarians and Antipatharians.* Prof. Thomson, M.A., and others.
„ No. 26.—*Surgical Instruments in Greek and Roman Times.* J. S. Milne, M.A., M.D.
„ No. 27.—*Records of the Sheriff Court of Aberdeenshire.* David Littlejohn, LL.D. Vol. III.
„ No. 28.—*Flosculi Graeci Boreales.* Ser. II. Professor John Harrower, M.A.
„ No. 29.—*Record of the Quatercentenary*, 1906. P. J. Anderson.
„ No. 30.—*House of Gordon.* J. M. Bulloch, M.A. Vol. II.
1908. No. 31.—*Miscellany of the New Spalding Club.* Vol. II.
„ No. 32.—*Religious Teachers of Greece.* James Adam, Litt.D. (Gifford Lectures, 1904-06.)
„ No. 33.—*Science and Philosophy of the Organism.* Hans Driesch, Ph.D. (Giff. Lect., 1907.)
„ No. 34.—*Proceedings of the Anatomical and Anthropological Society*, 1906-08.
„ No. 35.—*Records of Elgin.* Vol. II. Rev. S. Ree. B.D.
„ No. 36.—*Pigmentation Survey of School Children.* J. F. Tocher, B.Sc.
1909. No. 37.—*Science and Philosophy of Organism.* Hans Driesch, Ph.D. (Giff. Lect., 1908.)
„ No. 38.—*Studies on Alcyonarians and Hydroids.* Prof. Thomson, M.A., and others. Ser. III.
„ No. 39.—*Publications of Scottish Clubs.* Professor C. S. Terry, M.A.
„ No. 40.—*Aberdeen Friars: Red, Black, White, Grey.* P. J. Anderson.
„ No. 41.—*Studies on Alcyonarians.* Professor Thomson, M.A., and others. Ser. IV.
„ No. 42.—*Records of Old Aberdeen.* A. M. Munro. Vol. II.
1910. No. 43.—*Musa Latina Aberdonensis: Poetae Minores.* W. K. Leask, M.A.
„ No. 44.—*Bulletins of the Aberdeen and North of Scotland College of Agriculture*, Nos. 1-14.
1911. No. 45.—*Records of Inverness.* W. Mackay and H. C. Boyd. Vol. I.
„ No. 46.—*Zoological Studies.* Professor Thomson and others. Ser. V.
„ No. 47.—*Subject Catalogue of the Phillips Library.*
„ No. 48.—*Zoological Studies.* Professor Thomson and others. Ser. VI.
„ No. 49.—*Anacreontic Poetry of Germany.* John Lees, D.Litt.
„ No. 50.—*Creeds and Confessions of Faith.* Professor W. A. Curtis, D.Litt.
„ No. 51.—*Aberdeen Alumni at Other Universities.* Part I. Professor J. Harrower, LL.D.
1912. No. 52.—*Royal Fishery Companies.* J. R. Elder, M.A.
„ No. 53.—*Zoological Studies.* Professor Thomson and others. Ser. VII.
„ No. 54.—*Flora of Banffshire.* W. G. Craib, M.A.
„ No. 55.—*Catalogue of Anthropological Museum.* Professor R. W. Reid, M.D.
„ No. 56.—*Physical Geology of Dee Valley.* Alexander Bremner, M.A., B.Sc.
„ No. 57.—*Flora of Siam: Dicotyledones.* W. G. Craib, M.A.
„ No. 58.—*Notes on Academic Theses.* P. J. Anderson.
„ No. 59.—*Gordons under Arms.* C. O. Skelton and J. M. Bulloch, M.A.
„ No. 60.—*Society of Advocates in Aberdeen.* J. A. Henderson, F.S.A.Scot.
1913. No. 61.—*Flora of Siam: Monocotyledones.* W. G. Craib, M.A.
„ No. 62.—*Aberdeen University Library Bulletin.* Vol. I.
„ No. 63.—*Genealogies of an Aberdeen Family*, 1540-1913. Rev. James Smith, B.D.
1914. No. 64.—*Zoological Studies.* Professor Thomson and others. Ser. VIII.
„ No. 65.—*Highland Host of* 1678. J. R. Elder, D.Litt.
„ No. 66.—*Concise Bibliography of Aberdeen, Banff, and Kincardine.* J. F. Kellas Johnstone.
„ No. 67.—*Bishop Burnet as Educationist.* John Clarke, M.A.
1915. No. 68.—*Territorial Soldiering in N.E. Scotland.* J. M. Bulloch, M.A.
„ No. 69.—*Proceedings of the Anatomical and Anthropological Society*, 1908-14.
„ No. 70.—*Zoological Studies.* Professor Thomson and others. Ser. IX.
„ No. 71.—*Aberdeen University Library Bulletin.* Vol. II.
1916. No. 72.—*Physiological Studies.* Professor MacWilliam, F.R.S., and others. Ser. I.

Physiological Studies

(First Series)

By

J. A. MacWilliam, M.D., F.R.S.
Professor of Physiology

J. E. Kesson, M.D.

G. Spencer Melvin, M.D.

James R. Murray, M.D.

Edward S. Edie, M.A., B.Sc.

UNIV. OF
CALIFORNIA

Printed for the University of Aberdeen
1916

QP6
P5

BIOLOGY
LIBRARY
G

CONTENTS.

PAGES

The Estimation of Systolic and Diastolic Blood Pressures. By Professor MacWilliam, Dr. Kesson and Dr. Melvin - - - - - - - - 1-4

The Estimation of Diastolic Blood Pressure in Man. By Professor MacWilliam and Dr. Melvin - - - - - - - - - 5-48

Diastolic Blood-pressure Estimations by the Auscultatory and Oscillation Methods. By Dr. Melvin and Dr. Murray - - - - - - 49-63

Systolic and Diastolic Blood-pressure Estimation, with Special Reference to the Auditory Method. By Professor MacWilliam and Dr. Melvin . 65-77

Systolic and Diastolic Pressures in Aortic Regurgitation. By Dr. Murray 78-86

On the Resistance of Trypsin Solutions to Heat. By Mr. Edie - - 87-94

Action of Pepsin and Trypsin on One Another. By Mr. Edie - - - 95-105

Cardiac Fibrillation and Its Relation to Chloroform Anæsthesia. By Professor MacWilliam - - - - - - - - - - 107-112

Some Observations on Blood-pressure. By Dr. Melvin and Dr. Murray - - 113-116

Some Observations on the Significance of Blood-pressure Readings in Man. By Professor MacWilliam and Dr. Melvin - - - - - 117-130

Blood-pressure Estimation in Children. By Dr. Melvin and Dr. Murray - 131-135

422611

UNIV. OF
CALIFORNIA

THE ESTIMATION OF SYSTOLIC AND DIASTOLIC BLOOD-PRESSURES

BY PROFESSOR J. A. MACWILLIAM, J. E. KESSON, AND
G. SPENCER MELVIN

SYSTOLIC PRESSURE

Influence of the arterial wall. Living excised arteries were used in various states of contraction and relaxation—thickened arteries of old age and morbid conditions as well as those of normal adult animals. Surviving arteries from the legs of old horses provide valuable material in this connexion, being of great vitality and commonly thickened. The vessels were perfused with Ringer's fluid, a continuous or a pulsatile stream at different temperatures, and the relations of the external and internal pressures determined when the former was just sufficient to cause obliteration or to allow recommencement of the flow. The results were correlated with those obtained in blood-pressure estimations in man.

It was found that relaxed arteries, whether normal or thickened, showed no important resistance to compression. On the other hand, strongly contracted (e.g. by $BaCl_2$) and especially thickened arteries offered much resistance, particularly at the first test, amounting sometimes in the horse's metacarpal to over 60 mm. Hg, and in the normal sheep's carotid to 10–36 mm., at body temperature; to over 100 mm. in the former artery at room temperature.

Repeated compression or continued local compression or massage of the artery induced no change in the obliteration readings from normal arteries, but had great effect in lowering the readings from contracted or resistant arteries, the extent of such lowering varying according to the amount of resistance present and the extent and duration of the compression. Recovery, more or less complete, occurs after an interval. This affords a valuable method of ascertaining the presence of resistance in the arterial wall, though it does not discriminate between resistance (*a*) due to contraction of the media or (*b*) dependent on other causes (e.g. treatment with formalin, &c.).

In the great majority of blood-pressure estimations in man the arterial wall offers no important resistance, and introduces no appreciable error. But in some instances, in old people and others with contracted and thickened arteries, the first reading may be a very fallacious one. In these cases repeated or continued compression gives results strikingly similar to those obtained with excised arteries—marked lowering of the original values with recovery after an interval, &c. These results are indicative of the presence of marked resistance offered by the arterial wall against compression from without. Thickened and resistant arteries may fail to show such resistance, when there are soft non-resistant portions even of very limited extent in the area compressed by the armlet.

Conduction of the pulse wave. Two factors were distinguished :

1. The size of the lumen.
2. The elasticity of the arterial wall.

(1) Our experiments show that in arteries with a lumen less than a certain small size (e. g. 1 mm., &c.) there is a marked lowering of the obliteration readings ; this is a serious objection to the use of small arteries for blood-pressure estimation.

The same applies to larger arteries in which the lumen is very greatly narrowed by extreme thickening and contraction. Here there are two factors acting in different directions, the resistance of the arterial wall tending to exaggerate the obliteration reading and the smallness of the lumen tending to lower it by cutting down the systolic wave. When the brachial artery is tested the latter influence can rarely, if ever, come into play with appreciable effect.

Extreme constriction may cause complete temporary occlusion of arteries, resisting a perfusion pressure of about 400–500 mm. Hg, the condition determining intermittent claudication in the horse and in man.

(2) To test the influence of arterial elasticity, arteries contracted, relaxed, stiffened, and highly distensible were compared with rigid tubes. Rigidity of wall, as compared with a highly distensible and elastic condition, was found not to have any appreciable influence under conditions resembling those of blood-pressure estimation in man, the systolic wave being estimated by a similar obliteration test and by valved manometers. Even with highly distensible vessels and low diastolic pressures there is no progressive diminution of the systolic wave as it travels along the main arterial trunk of the upper limb. This holds good both in the normal subject and in such conditions as aortic regurgitation, with a very large systolic wave and a low diastolic pressure.

Inequality of obliteration readings from the arms. Apart from the remarkable arm-leg differences seen in certain conditions (e. g. aortic regurgitation) there is sometimes marked inequality between the two arms.

These readings can be more or less completely equalized by continued compression, the higher reading being reduced to a greater or less extent. The first reading would in such cases be a very fallacious one, varying according to the limb or portion of a limb examined.

Which is the more approximately correct reading and the truer indication of aortic pressure, the reading before or after local compression of the artery, the reading from the limb which has been influenced by such compression, or that which has not? Are these changes such as to cause the obliteration reading from a limb to approach more closely to or to diverge more widely from the actual systolic pressure in the aorta? The answer depends on the nature of the changes induced by the compression. If the alteration is due to more or less complete removal of resistance to compression in the arterial wall, the lowered reading is obviously the more correct one. On the other hand, if the conduction of the systolic wave has been markedly impaired, the subsequent obliteration reading would be more removed from the actual aortic pressure. We have seen that the evidence controverts the latter assumption—that variation in the conducting power of the arterial wall is of no practical importance in this connexion.

Diastolic Pressure

Maximum oscillation method. A circulatory schema was used with an artery in a compression tube or plethysmograph, valved manometers proximally and distally, volume records made graphically, &c.

Maximum oscillation according to the current view is an indication of diastolic pressure, the theory being that when the internal diastolic pressure is counterbalanced by an equivalent external pressure the distended artery returns to the size of the passive tube when empty or at zero pressure—what we designate the zero position—and is then in a condition to show the greatest expansion at the next systolic wave.

We find that the volume changes during maximum oscillation are made up of pulsatory changes in (1) the diameter and (2) the length of the tube subjected to compression. In regard to (1) the conditions are different according as (*a*) a normal distensible artery or (*b*) a practically non-distensible one is tested. In (*a*) volume changes induced by alterations of internal or external pressure are most extensive when the artery is in the half-flattened position between the pulsations—much more extensive than with the artery in the zero position. The half-flattened position is the optimum one in the normal distensible artery, but not in a non-distensible tube; in the latter (*b*) complete or almost complete flattening is required.

The excess of external pressure above the true internal diastolic pressure, needed to restore the optimum position in the time available between the beats varies according to circumstances, state of arterial wall, form of pulse-curve, rate of pulsation, &c. Pulsatory volume changes depending on (2) alterations in the length of the artery vary according to the state of the vessel as regards stretching between its attachments, contraction and relaxation, &c. Such alterations are not sufficiently covered by the animal experiments that have been made by various workers.

Maximum oscillation occurs with the external pressure at varying heights above the actual diastolic pressure in the artery and over-estimates the latter—often to a serious extent. The sudden decline in the oscillation magnitude which serves as an indication of the diastolic pressure, the Recklinghausen-Erlanger index, is often dubious or unrecognizable.

The auditory method. Tested by similar schematic arrangements and using wide variations in the conditions—height of pressures, amounts of pulse-pressure, rate of pulsation, &c.—the auditory method has given remarkably definite and precise indications of diastolic pressure, taking as the index the point where the sound suddenly diminishes in the course of gradual lowering of the armlet pressure. The sounds are produced by vibration in the artery compressed by the armlet, not much, if at all, by changes in the distal portion to which they are at present attributed.

The limitations and sources of fallacy in this method are few and easily guarded against. Insufficiency of flow through the artery and conduction along bone are possible sources of error.

Errors in the estimation of diastolic pressure by the auditory method are always associated with errors in systolic estimation by the same method; the latter can easily be detected by comparison with the tactile method. We recommend the combination of systolic and diastolic estimation by the auditory method with the ordinary tactile method, as verifying the validity of the auditory method as applied under the conditions that may be present in any particular instance. In the case of contracted or thickened arteries the method of local compression should also be used to eliminate as far as possible disturbing effects due to unusual conditions of the arterial tube. A nearer approach to the true pulse-pressure range is thus obtained. Erroneous estimates of the latter have often been due to systolic over-estimation from the cause already stated, or to diastolic over-estimation by the method of maximum oscillation. The pulse-pressure is much greater in many instances than is commonly believed.

It is clear that the auditory method must supersede the maximum oscillation method and others that have been proposed—based on the recognition of changes in the artery distally to the armlet; the last named we have found to be unreliable. The maximum oscillation method in its best form is relatively elaborate and cumbrous, subject to many causes of variation, dubious in its indications in many cases, and quite unnecessary in view of the simplicity and reliability of the auditory method. In the latter the diastolic index is a sudden weakening and dulling (not the extinction) of the sound.

THE ESTIMATION OF DIASTOLIC BLOOD-PRESSURE IN MAN.

By J. A. MACWILLIAM AND G. SPENCER MELVIN.

(*From the Physiological Laboratory, Aberdeen.*)

The importance of a knowledge of the diastolic pressure need hardly be emphasised, bearing in mind the valuable indications it may afford as to the peripheral resistance, the help it may give in interpreting the conditions of the circulation through its relation to the systolic pressure (pulse-pressure range), and the significance of its direct influence on the arterial walls (as the continuous distending force which they bear) and on the aortic valves.

Little attention is at present given to diastolic pressure in view of the prevailing opinion that there is no reliable and practicable method of ascertaining it, existing methods being difficult of application and uncertain as regards interpretation. Even as regards normal men diverse values have been stated as standards of diastolic pressure by different observers, and similar diversity of opinion naturally results as to the actual range of pulse-pressure in different conditions.

PART I.

THE MAXIMUM OSCILLATION METHOD.

Before entering on the consideration of the maximum oscillation method, some other plans which have been proposed may be briefly referred to. Masing[19] made sphygmograms from the artery distally to the armlet, and took the armlet pressure at which the maximum excursion of the sphygmographic lever occurred as the indication of diastolic pressure. Strassburger's[27] method is to raise the pressure in the armlet gradually and determine by palpation of the artery below when the pulse begins to feel smaller. Ehret[4] used a similar plan. Sahli[25] and Bingel[1] based their estimations on graphic records from the artery distally to the armlet. Observations on the foregoing plans have been made by many observers.

But in these methods the changes taken as indicating diastolic pressure are difficult of determination and interpretation. It is true that there are decided pressure changes in the artery distally to the armlet when the pressure in the latter is gradually raised or lowered. In our experiments such changes, as indicated manometrically, did not usually coincide with the internal diastolic pressure, but occurred while the external pressure was at higher levels; there was considerable variation in the precise relation of such changes to the actual diastolic pressure. These points are stated later in this paper. (See pages 15 & 16.)

The chief forms of apparatus used for the study of maximum pulsation are those in which pressure is applied to a limb by means of an armlet which is connected with an indicator of some kind. The latter may be arranged to yield visual indications, the magnitude of the oscillations being judged by the eye, as in Hill and Barnard's[11] larger apparatus, the compressed-air manometer of Oliver,[21] the oscillometer of Pachon,[22] and the mercury manometers of Stanton's[26] and of Janeway's[13] apparatus, &c., these latter being applications of Gumprecht's[10] observations that the oscillations of the Riva Rocci apparatus could be used for this purpose. Or, graphic records may be obtained by Gibson's[8] apparatus with Singer's modification, by Recklinghausen's[23] apparatus, and by the well-known Erlanger[5] sphygmomanometer.

The simpler forms in which pressure was applied locally over an artery as in von Basch's apparatus, Hill and Barnard's pocket sphygmometer, Oliver's hæmadynamometer, &c., have now been superseded by the above-mentioned types.

Views as to the significance of maximum oscillation.

As to the interpretation of the data provided by the maximum oscillation method there has been wide diversity of opinion.

Marey[17] introduced a new criterion for the estimation of blood-pressure by ascertaining the external pressure at which maximum pulsation occurs; he enunciated the principle, commonly designated by his name, that when the pulsations become maximal the pressure outside the artery must equal that within the vessel.

This principle of estimation, characterised by Janeway as unquestionably our most exact indirect measure of a blood-pressure, was applied by Mosso[20] in his sphygmomanometer; the latter investigator offered experimental proof of the theoretical accuracy of the method. He experimented with two vessels communicating by an opening closed by an unstretched elastic membrane. But such conditions differ widely from those present in the arteries used for blood-pressure estimations in man. Mosso believed that it was the mean pressure that he estimated by his sphygmomanometer.

Roy and Adami[24] concluded that the pulse-wave, as tested by their experimental sphygmometer, attained its maximum size when the extra-vascular pressure reached a height which just exceeded the minimum intra-vascular pressure. These observers applied local pressure to the radial artery by a small bag filled with water, a method now known to be attended by many sources of fallacy.

Hill and Barnard thought that the instruments devised by them indicated the mean pressure, and were confirmed in this opinion by experimentally testing a dog's thigh with an armlet and a pocket sphygmometer, the indications of the latter as regards maximum oscillation being compared with the readings of a mercury manometer connected with a cannula in the other femoral artery. They obtained corresponding values.

C. J. Martin[18] confirmed this experimental finding as to the relation of maximum oscillation to mean blood-pressure. He found that Hill and Barnard's small sphygmometer and Oliver's hæmadynamometer gave sufficiently accurate indications of mean pressure when applied to a length of exposed artery lying on a flat resistant surface, but not under conditions more nearly comparable to those present in the human subject. With the armlet also, even when filled with water, connected with a mercury manometer, he obtained dubious and variable results. Martin expresses a strong opinion " that the maximum systolic is the only point in the varying pressures of the cardiac cycle which can be determined with any degree of accuracy without opening an artery."

Sahli[25] regarded maximum oscillation as an indication of diastolic pressure, while Tschlenoff[28] associated it with systolic pressure.

Howell and Brush[12] fixed diastolic pressure as the phase of intra-arterial pressure to which maximum oscillation corresponds, at least under experimental conditions with an exposed artery subjected to circular compression. They enclosed a carotid artery (dog) in a glass tube and used valved manometers to show the intra-arterial pressure in the other carotid, &c. The artery examined was closed distally by being tied or connected to a manometer.

Howell and Brush's result is in accordance with Marey's principle, and it has been the accepted view since their investigation that maximum oscillation indicates diastolic pressure; this conclusion has been applied in the large amount of clinical work that has been done on the subject with the various forms of apparatus used, such as those of Erlanger, Oliver, Janeway, Gibson, Pachon, and Recklinghausen—the two last named being largely employed on the continent.

At the same time it is noteworthy that there has been so marked a conflict of evidence obtained by skilled observers (Hill, Martin, Howell and others) in regard to the manometric verification of the indications afforded by maximum oscillation—as to whether it is the mean or the diastolic arterial pressure that is indicated.

Oliver, who had for some years regarded maximum oscillation as indicating diastolic pressure, has recently inclined to the view that mean pressure may be the one indicated.

Mackenzie[15] believes that there is no definite point in the series of oscillations obtained with rising and falling external pressures that can be taken as an indication of diastolic pressure.

The diastolic index.

With the forms of apparatus in which the maximum of the oscillation has to be judged by the eye difficulty has been very generally felt in determining the optimum excursion, and anything like a precise definition of this is indeed very often impossible as the oscillations may look maximal over a considerable range of the external pressure which the instrument exerts upon the artery.

The same holds good when a graphic record is obtained, not only when air is used as the transmitting medium to the Hg. manometer, as in the instruments of Erlanger and Gibson, but even when the armlet and the connecting tube to the manometer are filled with water, as was done by Martin whose tracings show practically maximal oscillation over a considerable range of pressure with the oscillation magnitude tailing off above and below. Martin recommends (for estimating the *mean* pressure) raising the external pressure till it is certain that the oscillations diminish and recording this point, then lowering the external pressure till an undoubted diminution takes place; the mean between these two points to be taken. Gibson also recommends the taking of the middle point in the period of maximum oscillation, which is commonly an extended one in the tracings yielded by his apparatus; this is to meet or minimise a source of fallacy depending on the inertia of the mercury, as suggested long ago by Marey. While the pressure in the armlet is being continuously lowered (method of continuous escapement) the falling mercury carries the lowest point of maximum oscillation in the manometer down too far; hence Gibson prefers the middle point to the actual lowest point of maximum oscillation.

Recklinghausen, on the other hand, associated the lowest point at which the oscillation is maximal with the minimal intra-arterial pressure, *i.e.*, just before the abrupt diminution in the size of the oscillations which he found to occur as soon as the extra-vascular pressure fell below the diastolic pressure within the artery.

Erlanger interprets the tracings got with his sphygmomanometer by taking the point of maximal oscillation or the lowest point at which the oscillation is maximal (Recklinghausen's index) as a measure of the diastolic pressure. He states that when proper precautions are observed these two points usually coincide. But in the experience of many observers this point is often not at all definite, and opinions may differ markedly as to the precise point to be selected. On submitting tracings taken by this method to different observers, we have often found much diversity in regard to the point chosen, and in many cases great difficulty in deciding upon any point at all. In other cases the sudden diminution is quite well marked and affords very definite and valuable indications.

PRELIMINARY EXPERIMENTS.

Before proceeding to investigate the conditions and significance of maximal oscillation by means of a circulatory schema, we experimented on arteries to determine (1) the behaviour of their walls when compressed by definite increments of external pressure, and (2) the effects on the arterial volume of definite rises of internal pressure acting on arteries that are under the influence of different amounts of external pressure. Arteries being tubes of very special structure and properties, it is essential to use these in the living state, tested in different conditions; experiments with rubber tubes, &c., are on a different footing altogether.

Behaviour of the arterial tube when subjected to external pressures.

The behaviour of the arterial tube under the influence of external pressure was tested by placing a portion of artery in a plethysmograph or compression tube filled with oxygenated Ringer's fluid, in which the external pressure (*i.e.*, the pressure on the external surface of the artery) could be increased at will, the amount of such pressure being indicated by a mercury manometer. One end of the artery was closed by its being tied on a glass or wooden rod which passed through one of the rubber corks of the compression tube ; the other end was connected with a long horizontal tube of small calibre passing through the other cork. The artery was filled at zero pressure with Ringer's fluid which also extended for a short distance along the horizontal tube. Raising the external pressure gradually compressed the artery ; the resulting displacement of fluid from its interior was read off on a millimetre scale placed alongside the horizontal tube. The plethysmograph and its contents were kept at approximately body temperature. The pressure was raised by increments that varied in different experiments, and at intervals of different duration—commonly 1 minute periods.

The results obtained varied according to the increments of pressure used as a test. (With *small* increments compressibility and distensibility differ.)

When rises of 5-10 mm. Hg. are employed, contracted and relaxed arteries show remarkable differences in behaviour. In the former the displacements are at first small, gradually increasing to a maximum and then declining.* (Fig. 1.) In the relaxed vessel the first rise of external pressure causes the maximum effect—followed by diminishing effects on the cubic capacity of the tube. (Fig. 2.) These effects strikingly resemble the changes in capacity produced by similar increments of internal pressure in contracted and relaxed arteries respectively, as described by one of us (J. A. MacW.) many years ago. With certain tests the compressibility of the vessels seems to be closely comparable to their distensibility, at least as far as the broad features of their behaviour are concerned ; the processes of compression from without and distension from within show notable similarity in their development.

But such increments of external pressure as 5-10 mm. Hg., while quite suitable for contracted arteries presenting considerable resistance to flattening, are much too large to serve as an accurate test for relaxed arteries, the first increment being sufficient to flatten the vessel along almost its whole length without affording an opportunity for the behaviour of the tube at the different phases to be analysed. Consequently we have tried very small rises of pressure measured by a water-manometer, *e.g.*, 10-20 mm. H_2O. With such small increments a very different picture is obtained—a gradual increase in the changes of cubic capacity up to a maximum, followed by a declining series, *i.e.*, a behaviour similar in character to what occurs with a contracted artery, differing only in regard to the pressures required. (Fig. 13.)

---

* The final phases approaching complete obliteration when the displacements become extremely small are not to be regarded as accurately indicating changes in the tube as a whole. For at this stage the changes are chiefly near the ends kept open where tied on the glass tube or rod, when the rest of the artery has become obliterated.

Similar features are evident when an india-rubber tube is tested in the same way, large increments of external pressure being used in this (resistant) tube. (Fig. 4.) Such features are evidently common to tubes in general.

It is clear that the resistance of the tube (artery, &c.) is relatively high to begin with, when the circular form of the tube has to be distorted, and

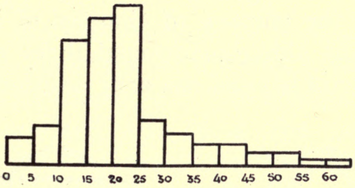


Fig. 1. Contracted artery. Volume changes caused by 5 mm. Hg. increments of external pressure.

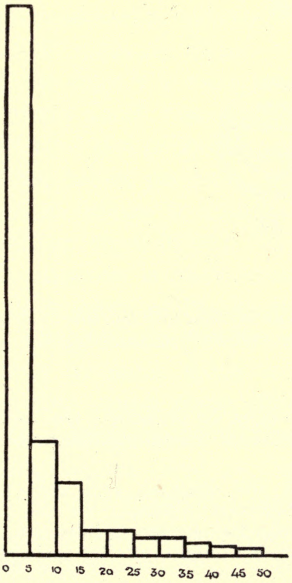


Fig. 2. Relaxed artery, Volume changes caused by 5 mm. Hg. increments of external pressure.

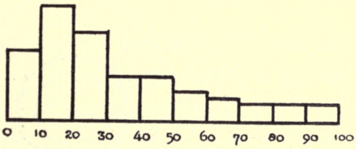


Fig. 3. Relaxed artery. Volume changes caused by 10 mm. H_2O increments of external pressure.

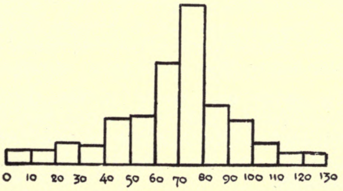


Fig. 4. Rubber tube. Volume changes caused by 10 mm. Hg. increments of external pressure.

that the maximum effect from equal increase of external pressure is got when the tube has reached an oval or half-flattened form. Small alterations of external pressure in this region would obviously give the greatest effect in the way of volume change.

Similarly, in the intact circulation changes in the veins from the oval to the circular form can readily provide a large increase in the capacity of the venous system with comparatively little alteration of internal pressure.

Volume changes caused by rises of internal pressure.

In this paper the term " zero position " is used to mean that of an artery in the normal circular form with zero pressure in its interior, *i.e.*, undistended. By " half-flattening " is meant such an approximate amount of flattening as is present when the shorter diameter is roughly about one-half that of the tube in its circular form. In " complete flattening " the sides of the vessels are opposed to one another with more or less complete obliteration of the lumen. (Fig. 5.)

We have compared the efficacy of changes of internal pressure acting on the arterial tube in the above-mentioned three positions and also when distended to various extents beyond the zero position.

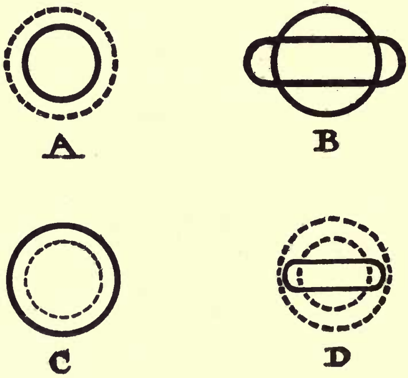


Fig. 5.

A. The continuous circle represents the zero position, and the broken line the diastolic position, the artery being expanded to a considerable (though variable) extent by the diastolic pressure within it.

B. The zero and the half-flattened positions are shown.

C. The continuous line represents the artery distended by diastolic pressure ; the broken line (zero) position to which the vessel returns when the internal diastolic pressure is counterbalanced by the application of external pressure.

D. The outer and inner circles (broken lines) indicate the diastolic and zero positions respectively ; the continuous line indicates the half-flattened position. In the phase of maximal oscillation the arterial tube changes from the half-flattened into the diastolic position, and then becomes further expanded to a variable extent by the systolic rise of pressure.

We began with such small alterations of internal or external pressure as are necessary to change an artery from the circular to the half-flattened position or *vice versa*. With an artery in the compression tube in the usual way we measured the amount of fluid displaced from it when half-flattening was caused by raising the external pressure to a sufficient extent. The artery was, to begin with, filled with fluid at zero pressure ; one of the tubes leading from it was closed, while the other communicated with a horizontal glass tube of small calibre fitted with a millimetre scale. The displacement of fluid from the interior of the artery was measured by its movement along the horizontal tube. With a relaxed or slightly contracted artery (*e.g.*, carotid of sheep) a very small pressure sufficed to cause half-flattening and a considerable volume change. Taking off the external pressure of course caused a return to the circular form with the same volume change ; the same result followed a similar small rise of internal pressure—to counterbalance the external pressure which had caused half-flattening.

In this way the amount of pressure necessary to change the vessel from the half-flattened to the circular form and the volume change resulting therefrom were ascertained.

The effects of such small alterations in pressure were then tested by experiments in which the same rise of internal pressure from zero or from various levels above zero was induced. The change in the external volume of the artery was determined by using the compression tube as a plethysmograph, one of the branches of its side tube being closed and the other connected to a horizontal glass tube with a scale. The expansion caused by a certain rise of internal pressure was read off on this scale. As the pressure alterations involved were small in the case of such an artery as the relaxed carotid of the sheep (*e.g.*, 2 mm. Hg. or less) a water-manometer was used to measure them.

In this way it is easy to compare the changes in arterial volume caused by a certain small rise of internal pressure acting on the artery (*a*) in the half-flattened and (*b*) in the zero position, or (*c*) at various phases of distension beyond the latter position. Even in a relaxed and highly distensible artery the volume change is found to be much greater in (*a*) than in (*b*) and very much greater than in (*c*). In other words the effectiveness of a small rise of internal pressure is very much greater when starting with a half-flattened artery than when acting on one in the circular form at zero pressure. In a normal relaxed artery the completely flattened position is not nearly so favourable to start from as the half-flattened state. The small rise of pressure acts much more effectively on (*a*) than on (*b*), the volume change being often three or more times as great in the former as in the latter. In such comparisons exactly equal periods of time must be allowed before reading the results, as the expansion and recovery of an artery with rises and falls of pressure are processes requiring a considerable time for their completion, the after-extension, &c., of such tissues being important. The results are of course strictly relative.

The actual pulse pressure in the circulation is, however, very much greater than those small rises ; the amount needed to open up the half-flattened artery forms only a small part of the pulse-pressure. Hence the essential comparison is between the effect of a few mm. of pressure expended (*a*) in changing the tube from the half-flattened to the circular position, and (*b*) the effect of a similar rise of pressure in carrying out the last part of the expansion of the circular tube in the systolic phase beyond the zero position. Are the few mm. more effectively spent in doing (*a*) and so not being available for (*b*), the amount available for distending the tube from the zero position being the pulse-pressure *minus* the few mm. in question? Is the pulse-pressure more effective when starting from the half-flattened or the zero (circular) position?

Assuming the pulse-pressure to be 40 mm. and 5 mm. to be necessary to open up the half-flattened vessel to the circular form in the time available, there will be 35 mm. available for distension from the zero position. In the other case, starting from the zero position the whole 40 mm. will act on the circular tube. Are the 5 mm. more effective in the former case than in the latter, when serving as the final increment in distending the circular tube? The more the artery is distended—assuming it to be a relaxed or a slightly contracted one—before the final increment of internal pressure comes into action, the less effect it will have since it becomes less distensible at high pressures, the co-efficiency of elasticity increasing greatly.

A strongly contracted artery would yield more *relatively* at higher increments but the *actual* change would be very small, in the brief time that the pressure rise acts. Such transient rises have little effect in expanding a strongly-contracted artery; the process of expansion goes on slowly and a considerable time is necessary for the manifestation of anything approaching the full effect which a certain increment of pressure may be capable of exercising upon the arterial wall.

We tried the effects of systolic rises of values resembling those of the pulse-pressure in the circulation, starting from (*a*) the half-flattened position, and (*b*) the zero position, &c. The former position (*a*) is established by the pressure of a column of fluid of sufficient height, this fluid being contained in a tube connecting the side-piece of the compression tube with the horizontal measuring tube, which in this case was placed on a level elevated to a suitable extent. Such experiments were made with arteries in various conditions, with results that were always of the same nature, the advantage as regards the magnitude of the volume oscillation always being associated with (*a*). This holds good even when with an extremely distensile artery which expands extensively both transversely and longitudinally when starting from the zero position (*b*). An extreme case of such an artery was obtained by using an ox carotid which had been softened by exposure to ammonia vapour for some minutes. With an internal rise of 30 mm. the expansions in (*a*) and (*b*) bore the ratio of about 130 : 80; with a rise of 70 mm. such ratio as 35 : 23, &c., the volume change from the half-flattened position being thus about half as great again as from the zero position, even with so abnormally distensible a vessel. With less distensibility a still greater advantage rests with (*a*).

All the foregoing experiments give results which concur in showing that in such distensible tubes as normal arteries, relaxed or in a state of moderate tone, the half-flattened position is the optimum one for a systolic expansion to start from. In relatively non-distensible vessels, whether strongly contracted or pathologically altered, a greater degree of flattening is found to be advantageous.

The pressure changes tested in these experiments are of considerable duration (1 min., &c.). The results are indicative of important differences in the behaviour of the arteries in various conditions, and the presumption is that a broad similarity of behaviour must be manifested in the different time relations that are present in the human circulation. To obtain further evidence, experiments with pressures varying at rates comparable to those in the circulation were carried out by means of a schema.

EXPERIMENTS WITH A PULSATILE SCHEMA.

Using a compression tube of the type already described, we placed in it a length (10-14 cm.) of contracted or relaxed artery, tied on glass tubes of similar calibre which passed through the rubber corks of the compression tube. Valved manometers (maximum and minimum) were connected near the proximal and distal ends of the compression tube, connections of equal calibre and length being used. Spring outlets were employed to regulate the peripheral resistance. Ringer's fluid was used as the perfusing fluid, and the same filled the space around the artery and the tubes leading to the manometers. The general arrangement is indicated in Fig. 6.

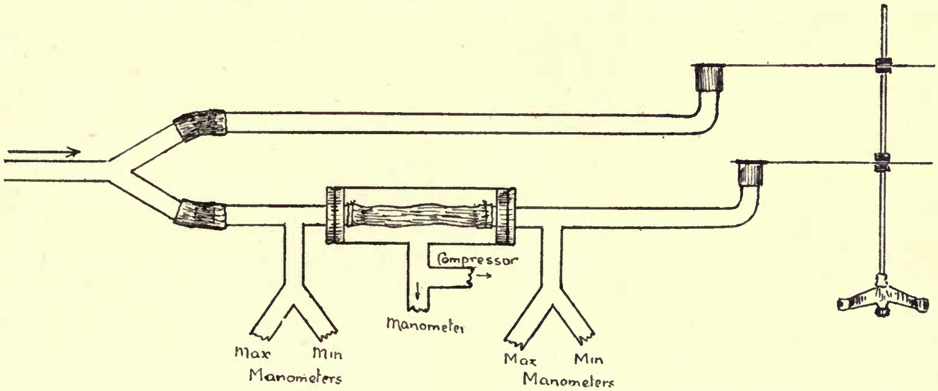


Fig. 6. Arrangement for studying maximum oscillation in an excised artery. The proximal and distal pairs of manometers (maximal and minimal) are connected near to and at equal distances from the ends of the artery in the compression tube. The side tube of the compression tube or plethysmograph communicates with a Fick manometer or other recording apparatus, as well as with an Oliver's screw compressor. Tested separately the Fick manometer gave, with pressures up to at least 160 mm., practically equal excursions in response to equal increments of internal pressure.

The external pressure around the artery in the compression tube was raised by a compressor, usually Oliver's screw compressor; connected by a T piece with the same branch of the side tube of the compression tube was a mercury manometer to indicate the height of the internal pressure. The other branch of the side tube led to a Fick manometer, used to record the oscillations of the arterial volume. When tracings were being taken the compressor was shut off by a stop-cock between it and the compression tube; a stop-cock between the latter and the Hg. manometer was turned just enough to allow the pressure changes to show in the Hg. manometer while not cutting down the oscillations in the Fick much. This stop-cock when once arranged was left unchanged during a series of observations.

By this method graphic records of oscillation were got, with measurements of the internal pressure (systolic and diastolic) on both the proximal and the distal aspects of the artery under examination, while the vessel itself was studied by direct inspection and the changes apparent in it were correlated with the variations in the oscillation, the internal pressures, the relation of the latter to the external pressure around the artery, &c.

In a number of experiments the Erlanger recording apparatus was used, being connected with the compression tube instead of the Fick manometer; air was commonly used as the transmitting medium in these experiments. The main results were essentially similar to those obtained with the Fick manometer, though there were some differences in detail.

To establish the relation of maximum oscillation to internal pressure is by no means a simple matter in an experimental schema.

Some investigators have used an ordinary Hg. manometer and have drawn conclusions as to the relations of the external pressure (at which maximum oscillation occurs) and the internal diastolic and systolic pressures, evidently overlooking the serious nature of the errors that may arise from the use of a simple Hg. manometer for this purpose—errors varying not only in amount but in their nature, under the influence of different rates of pulsation, &c.

Martin measured the internal pressure in his experimental schema by an ordinary recording Hg. manometer. Erlanger used a maximum and minimum manometer placed on the proximal side of the tube, &c., under examination; on the distal side he used in some experiments a mercury manometer to record the pulsations passing through.

The existence of constrictions at any part of the channel has to be carefully guarded against. We tie glass tubes of uniform calibre into the arteries, not cannulas with constricted necks. Torsion of the artery and disturbance of the arterial tube that may result from ligaturing branches too close to their origin have also to be avoided. Leaks in the vessel have been tested for by air pressure.

The external pressures are inscribed above the tracings, with the exception of Fig. 17. The internal pressures are marked below the tracings, those on the proximal side, systolic and diastolic, as Prox. $\left\{ \begin{matrix} \text{S.} \\ \text{D.} \end{matrix} \right.$; those on the distal side as Dist. $\left\{ \begin{matrix} \text{S.} \\ \text{D.} \end{matrix} \right.$

Measurement of internal pressure. It is necessary to obtain readings of systolic and diastolic pressures both proximally and distally to the artery in the compression tube, adjusting the valved manometers with each alteration of the external pressure. There may under some conditions be a considerable pressure gradient in the stream between the proximal and the distal manometers; in such a case the actual pressure within the artery is decidedly different from what is indicated by the proximal manometers. The artery may show flattening when subjected to an external pressure lower than the reading of the proximal minimal manometer, in which case there is obviously a fall of pressure between the proximal manometer connection and the artery ; this fall is shown by the lower reading in the distal manometer. If a steep gradient is present, the pressure varies considerably along the length of the artery, so that there is a definite external pressure acting on the whole of an artery which has differences of internal pressure at different parts of its course. We have usually arranged our schema so as to have comparatively slight pressure differences between the proximal and distal ends of the artery. The ends of the artery being equidistant from the manometer connections the actual pressure at the middle of the artery is obtained by taking the mean of the proximal and distal pressures. But considerable disturbances in the internal pressures and the relations of the proximal and distal pressures may be caused by the application of external pressure ; this is especially marked in regard to the distal pressures at a certain level upon gradual elevation of the external pressure. Up to a

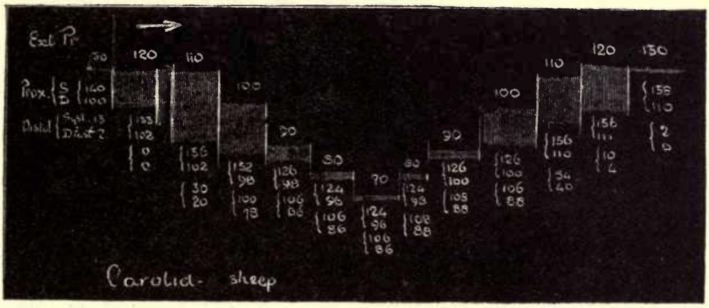


Fig. 7. The tracing is to be read from left to right. This artery had a strongly resistant wall. There is marked difference in the effects of a falling and a rising external pressure. The maximal phase is much above the actual diastolic pressure within the artery. The phase (90 mm.) of relatively small oscillation adjoining one of approximately maximal size, there being an abrupt change from one to the other, is nearer the diastolic pressure. The external pressures are marked above the tracing, the internal pressures below. The prox. systolic (S.) is immediately below the tracing, then the prox. diastolic (D.). Lower down come the distal systolic and the distal diastolic.

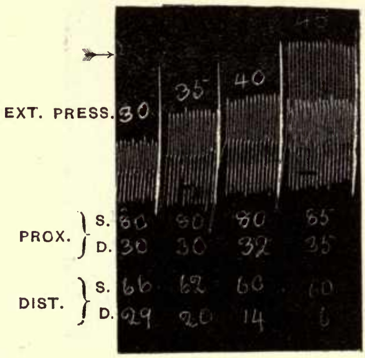


Fig. 8. Carotid, ox. With an external pressure equal to the internal diastolic the oscillation is relatively small. The maximal phase is not reached till the external pressure (45 mm.) is much above the internal. There is a marked fall in the distal diastolic at 35 mm. external pressure, very considerably before the maximal oscillation.

certain height there is little or no change in the distal pressures; then the latter become lowered very much, the diastolic pressure being extensively affected at an earlier phase than the systolic. The relation of distal to proximal pressures becomes greatly changed. (See Fig. 7, 8, 9, 11.)

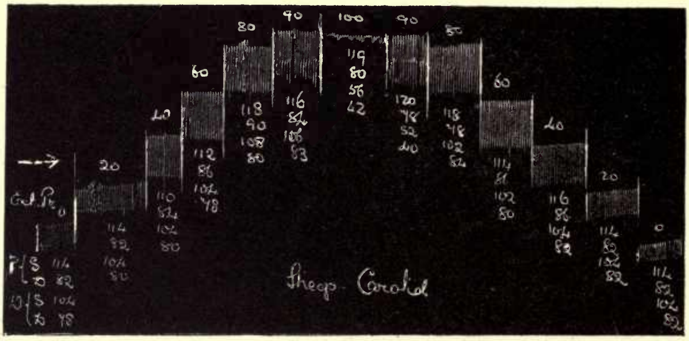


Fig. 9. The tracing reads from left to right. Relaxed artery. The oscillation shows a gradual change in size at different external pressures. The fall in distal diastolic pressure occurs at an external pressure higher than is necessary to elicit the maximum oscillation, and at different levels with a rising and with a falling external pressure.

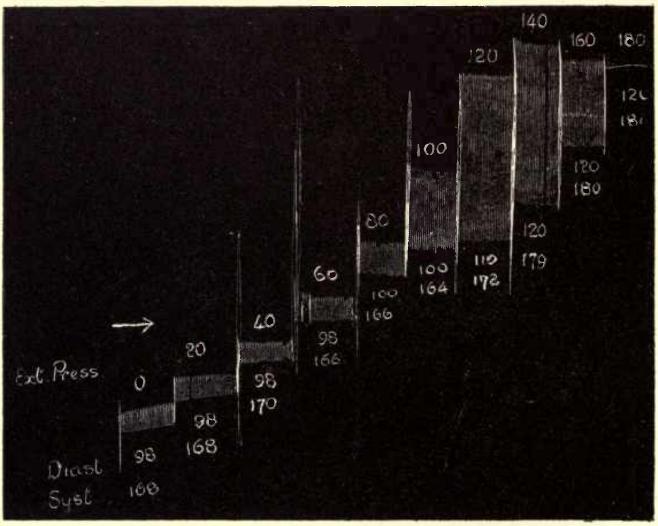


Fig. 10. Carotid, ox. The maximal phase is above the diastolic pressure indicated by the proximal manometer. The preceding phase corresponds to the proximal diastolic pressure (100 mm.); there is an abrupt change in size between this and the maximal phase. There is also an abrupt change between 100 and 80 external pressure.
The distal pressures are not recorded in this tracing.

After such disturbance has occurred the actual pressures present in the artery cannot with confidence be deduced from a comparison of the proximal and distal pressures; the mean between these two cannot safely be taken as indicating the pressure in the artery midway between the proximal and distal manometer connections. The relation of the occurrence of an extensive change of this sort to the phase of maximal volume oscillations varies. (1) The change is commonly established when the external pressure is raised sufficiently to induce the phase of maximum oscillation, though differences in this, as in other respects, may be seen in the same artery with rising and with falling external pressure. (See Fig. 7, 11.) (2) Sometimes the disturbance in the distal pressures begins and becomes well marked much lower than the phase of maximum oscillation (Fig. 8), corresponding pretty closely, it may be, with the internal diastolic pressure as indicated by the proximal manometer. (3) In other experiments (Fig. 9, 12, 13), no marked disturbance occurred until the external pressure had been raised to a point decidedly above the phase of maximum oscillation.*

We find that the changes in the internal pressures caused by the application of external pressure vary strikingly, according as the latter is applied (1) while the stream is flowing through the artery in the usual way, and (2) while the stream is stopped by clamping the tube beyond the connection of the distal manometers.†

In (1) the proximal pressures, both systolic and diastolic, usually tend to rise more or less distinctly though the change is not usually an extensive one ; above a certain level of external pressure the distal pressures, systolic and diastolic, fall very markedly, the diastolic being often extensively affected at an earlier stage than the systolic. (See Figs.)

In (2) the systolic pressures, proximal and distal, are lowered while the diastolic pressures, proximal and distal, become elevated. (Fig. 14.)

The foregoing effects of external pressure are of course most marked when a large artery (*e.g.*, carotid of ox, &c.), is tested.

The effects of external pressure upon the internal pressure are influenced to some extent according as to whether the air in the compression tube is, or is not, in continuity with the air in the Oliver's compressor, rubber bag, &c., used for raising the pressure. While continuity is present the effects are appreciably more extensive ; when the reservoir of air in the compressor is shut off there are notable differences in effect according as to whether it is shut off during the systolic or the diastolic phase, the influence of the latter approaching nearer to that present during continuity, *i.e.*, diminution of systolic and increase of diastolic pressures.

Turning off and on the Hg. manometer used to measure external pressure is in certain circumstances not free from some disturbing influence on the internal pressures.

In regard to the comparison of the size of the oscillations at different external pressures it is, of course, essential to record the exact amount of the pulse-pressure at each phase, varying to some extent as it may do under different conditions. Through the influence of a temporary increase of the range between the systolic and diastolic pressures (pulse-pressure) it is clear that oscillations of disproportionately large size might be got at a phase other than the optimum position of the arterial wall.

---

* The variation in the relation of these changes to the actual pressures throws grave doubt on the reliability of the various methods, based on the recognition of such changes, which have been proposed by different workers for the estimation of the diastolic pressure in man.

† In their experiments on animals Howell and Brush closed the artery (carotid) which they examined in their plethysmograph, by ligaturing it peripherally or connecting it to a manometer.

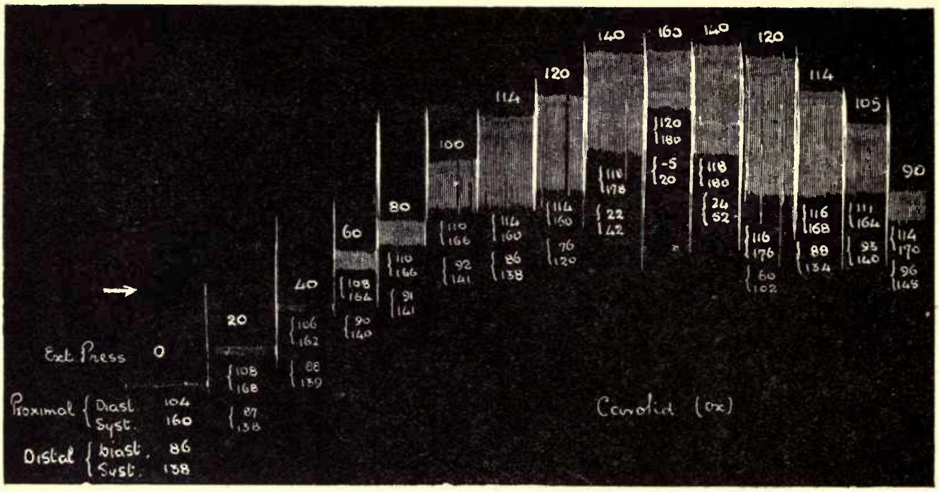


Fig. 11. The behaviour of the oscillation is different with the rise and fall of the external pressure, the size being greater during the fall and the maximum phase at 120 instead of 140 mm. external pressure. It is difficult to say which phase should be taken to represent the Recklinghausen index; there is no definite indication corresponding to the internal diastolic pressure.

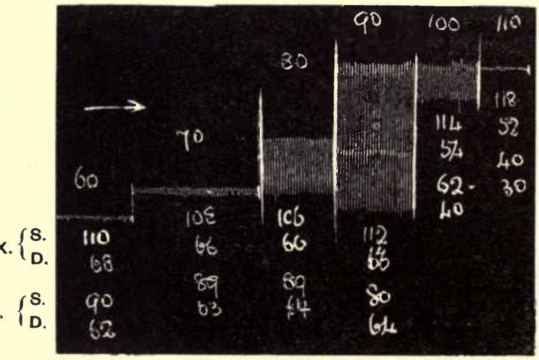


Fig. 12. Carotid, sheep (natural size). The phase of maximum oscillation (90 mm. external pressure), is much above the internal diastolic pressure. The preceding phase of much smaller oscillation is also at an external pressure (80 mm.) much too high.

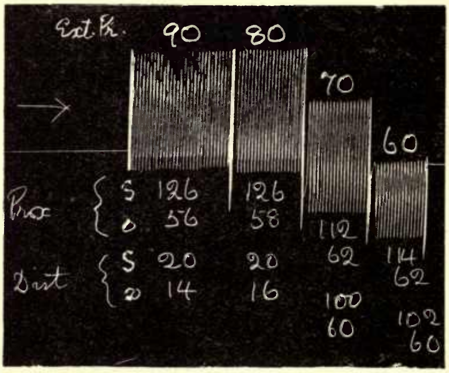


Fig. 13. Carotid, ox. Maximal oscillation occurs considerably above the internal diastolic pressure. The external pressure (60 mm.) immediately after the abrupt diminution from the approximately maximal size corresponds pretty closely with the internal diastolic pressure.

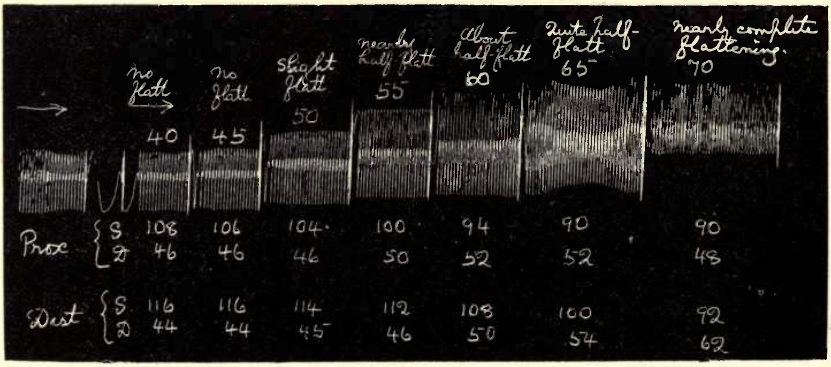


Fig. 14. Carotid, ox. The general relations of flattening to oscillation magnitude and internal pressures are shown in this tracing. It is to be noted that there was no stream flowing through the artery in this experiment, a clamp having been applied on the distal side—beyond the distal manometer connection. Application of external pressure leads to a fall of systolic and a rise of diastolic pressures, both proximally and distally.

Measurement of external pressure.

In comparing the extravascular and intravascular pressures and their relation to the development of volume oscillations the mode of measuring the external pressure is necessarily important. Is it the mean pressure or the minimum between the pulse beats that is to be taken? The latter is obviously the one that directly influences the size of the artery between the systoles—in the diastolic phase. With large pulse-pressures and a distensible artery pretty large variations in the external pressure occur at each pulse-beat, as seen clinically from the oscillations of the mercury in the apparatus of Janeway, Stanton, Gibson and others. Mean and minimal pressures must evidently have notably different values.

Erlanger in some experiments compared the measurements of external pressure in his plethysmograph—apparently with air transmission—by an ordinary Hg. manometer, and a minimum manometer; he obtained practically corresponding readings from the two, and he seems to interpret the readings as indicating minimum pressure.

With our circulatory scheme we have compared simultaneous readings by the Hg. manometer (compensated) and the valued minimum manometer under two conditions (1) with the space around the artery and in the tubes leading to the manometers filled with air, and (2) with Ringer's fluid replacing the air. Quite different results were yielded in the two cases. In (1) the minimum manometer gave lower readings than the mean of the ordinary Hg. manometer, but the differences were slight except when the volume oscillation was very extensive, the differences being more marked with the higher external pressures, and being trivial at atmospheric pressure when the air served as a highly compressible medium. For example, when the Hg. manometer showed a mean pressure of 58 mm. the minimum manometer reading was 50; when the former stood at 32 mm. the latter was 30 mm.

It is to be noted that a *mean* external pressure exactly equal to the internal diastolic pressure would not bring the artery to the zero position between the beats; a *diastolic* external pressure equal to the internal is necessary.

In (2) with an incompressible transmitting medium the movements in the Hg. manometer, when uncompensated, were of very considerable extent, varying of course with the pulse-pressure, and the size and distensibility of the artery. The minimum manometer gave a much lower reading than before, much below the mean pressure indicated by the compensated Hg. manometer, the discrepancy often being a very important one. When uncompensated the lowest point in the movement of the free-swinging mercury commonly did not coincide with the reading of the minimum manometer on account of the inertia error of the Hg. giving too low a value with a slow pulse and too high with a quick pulse.

RELATION OF EXTERNAL AND INTERNAL PRESSURES DURING MAXIMAL OSCILLATION.

In view of the complexity of the conditions affecting the volume oscillations, as stated later, it is not surprising to find very considerable diversity in the results. Much depends on what is taken as the measure of diastolic internal pressure—the pressure on the proximal side of the artery or the average between the proximal and the distal pressures. In regard to the latter the great disturbance which occurs with a certain elevation of the external pressures introduces great difficulty in determining the actual pressure in the artery lying between the proximal and distal manometer connections. Under such complex conditions as may be present here, we have not felt warranted in taking the average between the proximal and distal readings as indicating the true pressure in the interior of the artery. We have relied rather on experiments in which the disturbance referred to had not occurred on raising the external pressure sufficiently to elicit maximal oscillation and where the differences between the proximal and distal readings were small, the pressure gradient being a slight one.

We find that the diastolic external pressure necessary to elicit maximal oscillation is always higher than the actual diastolic pressure within the artery; the difference is increased if the mean external pressure is taken for comparison. The excess of external pressure varies greatly, from a few mm. Hg. to 20 mm. or more ; it often amounts to about 10 mm.. (See Fig. 10-16.)

If the average between the proximal and distal pressures were used in the cases where a great fall in the distal pressure has been caused by the application of external pressure, the discrepancy between the external and internal pressures during the phase of maximal oscillation would of course be much greater.

The position of the maximal phase and the magnitude of the oscillations may vary with a falling as compared with a rising external pressure. (Fig. 7 and 11.)

When an abrupt change is evident in the decline of the oscillation magnitude from the large or merely maximal size such is commonly associated with an approximate equality of external and internal pressures, such equality being present when the external pressure has been lowered just sufficiently to give the characteristic reduction in oscillation magnitude which is oftentimes easily recognisable.

Condition of the artery during maximum oscillation.

Normal distensible artery. Direct observation of relaxed normal artery in the compression tube, while the external pressure around the vessel is being gradually raised or lowered and its pulsatory oscillations in volume are being graphically recorded, makes it very plain that the maximum oscillations do not occur (as is believed at present) when the external pressure is such as to cause the vessel to return to the condition of the passive artery (empty, or filled with blood at zero pressure) between the pulse beats. The present view, in accordance with Marey's principle, is that the volume change is greatest when the expansion starts from the condition of the "passive" artery, the circular unstretched tube being then ready to undergo the greatest enlargement during the systolic rise of internal pressure—the change being from a circular tube of smaller size to one of larger size. (Fig. 5A.)

Direct inspection shows that this view is not correct. The conditions just described do not by any means give the largest oscillations. When the external pressure is further raised, so as to cause an alteration in the form of the tube in the diastolic intervals, a certain amount of flattening or distortion from the circular form, a decided increase in the magnitude of the volume oscillations is seen. Maximal oscillation does not develop until flattening reaches such a degree that the shorter diameter of the tube is (roughly) something like half that of the passive circular tube—a condition to which, for convenience, we have applied the term "half-flattening."* (Fig. 5B.)

---

* A similar condition is probably present in a normal artery when a sphygmograph is applied and the maximum excursion of the lever is being obtained. That the vessel is by no means completely flattened between the beats is indicated by the fact that when the brachial artery is closed by digital pressure the sphygmograph lever sinks markedly.

When the external pressure is carried so high as to cause complete or nearly complete flattening of the artery between the pulse beats the oscillations are markedly diminished, the optimum point being decidedly exceeded.

When the external pressure is first raised to the obliteration point and then gradually lowered, a series of similar changes, in inverse order, is evident.

Nature of the volume changes in maximum oscillation.

We have found that this differs in two conditions :—

(1) In the normal distensible artery ;

(2) In non-distensible tubes ; and in arteries that are practically or relatively non-distensible at blood-pressure, on account of the presence of strong contraction or of pathological change.

Normal distensible artery. The volume increase represented by each oscillation is compounded of two portions :—

(*a*) The volume change caused by an alteration from the half-flattened to the circular form (zero position). (Fig. 5, B and D.)

(*b*) Expansion of the circular tube from the zero position towards or beyond the diastolic position, *i.e.*, the position of the arterial wall in diastole when the diastolic pressure is not counterbalanced by external pressure. According to the view at present accepted (*b*) is the only factor in the production of the oscillation. (Fig. 5, A and D.)

In the normal state when no external pressure is applied to an artery, its expansion at each pulse-beat is relatively slight, on account of the fact that the vessel is already very considerably distended by the permanent diastolic pressure and not easily distended very much more by the systolic rise.* It follows that if the artery is reduced to the zero position by counterbalancing the internal diastolic pressure by external pressure, the systolic pulse pressure would then, acting on the undistended tube, produce much more expansion than when it acts on an artery already distended to the diastolic size. This difference is one that would naturally be predicated in the case of a relaxed artery, from what is known as to the diminishing increments of volume caused by successive increments of internal pressure. In a contracted artery, on the other hand, the distensibility has been found to be greater at a phase when the vessel is already filled at considerable pressure—the amount varying according to the strength of contraction present. But this difference in a contracted artery is only relative, and the actual amount of distension (at any phase) induced by such quick and transient rises of pressure as those of the pulse waves is very slight ; this has been shown by direct experiment by one of us (J. A. MacW.) and is evidenced by the absence of visible systolic expansion of contracted arteries in the body even with a good pulse-pressure.

---

* Changes in length, straightening of curves and locomotion are commonly much more marked than transverse expansion.

While maximal oscillation is occurring, some of the systolic rise is being expended in changing the artery from the half-flattened to the circular form by overcoming the extra external pressure which was needed to induce the half-flattened position in the time available between the pulse beats.

All the rest of the systolic rise acts upon the now circular tube, distending it from the zero position to a greater or less extent according to the distending pressure available and the elastic resistance presented by the arterial wall. If the available pressure is equal to the original diastolic pressure the tube will be distended to the diastolic position ; if the available pressure is greater the distension will necessarily go further.

The comparatively small portion of the systolic rise that is spent in changing the half-flattened tube into the circular form is much more effectively used in causing volume change in this way than it would be by adding to the last phase of the expansion of the circular tube from the zero position ; in this last phase the effect of a little more pressure would be very slight as the artery is already considerably distended and the co-efficient of elasticity in its wall increased, at least as far as relaxed or slightly contracted arteries are concerned, while in strongly contracted arteries the whole expansion from the zero position (though relatively greater at higher pressures) is slight as compared with the volume change depending on alteration in the shape of the tube.

When the external pressure is raised to such a height that the artery is completely flattened between the beats the external pressure must equal the diastolic pressure *plus* the resistance which the tube offers against being flattened in the time available between the pulse-beats. In recovering (under the distending force of the pulse pressure) from complete flattening the elastic reaction of the tube fades away as the latter recovers, and as the external pressure remains undiminished some of the pulse-pressure must be used in increasing amount, to bring the tube back to the circular form ; from this point distension has to be carried on against an external pressure which is higher than in the case of half-flattening by the additional external pressure necessary to give the complete flattening. Even in so easily compressible a tube as the relaxed carotid of the sheep the difference in the size of the oscillations with (*a*) half-flattening and (*b*) complete flattening is quite marked, the oscillations being decidedly smaller in the latter, Evidently the excess of external pressure needed to cause complete flattening in the time available between the pulse-beats is sufficient to have a prejudicial effect on the size of the oscillations, interfering seriously with the amount of opening up and expansion of the distensible tube by each systolic rise. (Fig. 14.)

Development of oscillations when the pressure on the exterior of an artery is gradually raised. As the external pressure is increased, reducing the size of the artery between the beats, the oscillations grow in size till the zero position of the arterial tube is reached between the pulse-beats ; the distension at each beat approaches or reaches or overpasses the diastolic position according as the amount of the pulse pressure approaches or equals or exceeds the original diastolic pressure.

With further elevation of the external pressure partial flattening of the artery between the beats begins, and the oscillations increase, often with some suddenness, being augmented by the volume change involved in flattening and recovery of the circular form. With external pressure increments of 5 mm. Hg. the development of flattening is apt to be sudden, if the increment acts on a vessel already at the zero size. But if the last increment falls short of establishing the zero position say by 2 or 3 mm., then only 2-3 mm. of the next increment are available for causing flattening, and the increase in the size of the oscillations may not be so sharp. Much depends on the resistance offered by the arterial wall in relation to the periods during which the pressures act.

Non-distensible tube or artery. Here the only volume change possible is by flattening to various extents and the recovery from the same. The greatest possible displacement will of course be got with complete flattening, when the pulse pressure is sufficient to open (within the time available) up the tube to its original circular form against the external pressure necessary to cause complete flattening between the beats.

In such tubes we have found by experiment that the maximum oscillation occurs when the external pressure is raised to such an extent as to cause complete or almost complete flattening between the systoles ; this constitutes a notable difference from what obtains in a distensible artery. An external pressure sufficient to cause half-flattening of the non-distensible tube elicits oscillations that are by no means maximal ; the half-flattened position is not the optimum one here. With the complete or almost complete flattening the oscillations are maximal even when the systolic rise does not nearly open up the tube to its circular form between the beats. Further distension of the vessel after the circular form has been restored, which plays a very important part in the volume oscillations of normal arteries, is slight or absent here, according as to whether the loss of distensibility in the artery is more or less complete.

These facts have obviously an important bearing on the study of maximum oscillation in man. Normal arteries, when contracted, and pathological arteries with stiffened or relatively inelastic walls present numerous gradations in character between the highly-distensible and easily compressible tube represented by a normal relaxed artery and a more or less completely non-distensible tube, the latter, while non-distensible by internal pressure, being (*a*) in some instances easily compressible by external pressure, and (*b*) in other instances offering marked resistance to compression by external pressure. It follows, in accordance with the foregoing observations, that there must be, *caeteris paribus*, a similar variation in the behaviour of these different vessels as regards their pulsatory volume changes under the influence of external pressures.

Further it is to be borne in mind that in pathological conditions arteries are commonly very far from being uniform in character along their length, there being often large variations in shape, calibre, thickness of wall, stiffness, elasticity, &c. Reasoning based on the conception of such vessels as regular cylinders with walls of uniform character is obviously inapplicable in such cases.

Influence of a resistant arterial wall. It is obvious that the amount of resistance to compression offered by the arterial wall must affect the amount of external pressure necessary to cause the requisite amount of flattening in the time available between the systolic waves. Different degrees of resistance, along with defective distensibility, may depend on different degrees of contraction ; as has been described, contraction (or resistance from other causes) can be greatly reduced, if not altogether removed, by repeated or continued compression. The initial raising of the external pressure above the obliteration point, as in the Erlanger method, tends to reduce resistance offered by the arterial wall.

With arteries in the compression tube we have frequently obtained graphic records showing notable differences when taken with a rising external pressure as compared with those obtained during the subsequent lowering of the same pressure ; the differences affect both the position of the maximum phase and the size of the oscillations. With the lowering of the external pressure the maximum phase often comes at a lower level and with enlarged amplitude of excursion. This is probably due to the influence of the preceding compression on the arterial wall.

Martin recorded a result of this kind in the case of an old man with considerable arterial sclerosis, a failing heart and a high systolic pressure (200 mm.), where the maximum oscillation was obtained at the systolic level with the rising external pressure and considerably lower with the falling external pressure. He suggests no explanation of this, but remarks that such variation with the conditions under which the record is taken constitutes a serious indictment against the maximum oscillation method.

The occurrence of maximum oscillation at (or near) the systolic pressure (pulse obliteration), though agreeing with the (discredited) view of Tschlenoff, seems paradoxical. But such is quite conceivable in the case of an artery which is very compressible near its distal end, while resistant and non-distensible (*e.g.*, from strong contraction) along the rest of its length. With such an artery in the compression tube we have sometimes seen the maximum oscillation approaching the systolic (obliteration) level in a remarkable way ; the compressible distal end was closed by an external pressure not much above what was necessary to elicit maximal pulsation in the rest of the tube.

In this connection the position of the arterial wall when maximum oscillation occurs is evidently important. If a restoration of the zero position by external pressure is all that is needed, as is commonly believed at present, resistance of the wall to compression would not come into play—in contrast to the requirements of a flattened position. In accordance with the view at present held it has been asserted that the maximum oscillation method gives results that are unaffected by the state of the arterial wall. Such a conclusion is obviously unwarrantable.

Influence of the form of the internal pressure curve. If the internal pressure curve is of such a form that the minimal level of pressure is of extremely short duration a higher external pressure will, *caeteris paribus*, be needed in order to establish the half-flattened position between the beats.

Influence of pulsatile changes in length on the oscillation. This factor seems to have been entirely overlooked in the consideration of the question of maximum oscillation. In the application of Marey's principle the behaviour of the tube as regards transverse expansion is what has been discussed.

The volume change depending on pulsatile elongation of an artery varies much in different circumstances; under certain conditions, with no external pressure applied, &c., the increase from this cause is much larger than that due to transverse expansion, both in contracted and relaxed arteries, the actual volume change being vastly greater in the latter.

If an artery under the influence of the diastolic pressure is bent to one side, either before the systolic rise of pressure or during that phase, the longitudinal expansion is very striking. On the other hand an artery kept straight during the systolic phase by longitudinal tension shows only transverse expansion.

The normal longitudinal tension of an artery between its attachments is tension in an empty tube, the latter being shorter than the distance between its attachments. But the tube when stretched by a certain internal pressure is long enough to cover the distance without longitudinal traction, *i.e.*, with no pull upon its attachments; of course this involves longitudinal tension of the elements of the arterial wall though applied by internal (blood) pressure instead of external longitudinal traction applied at its ends or attachments.

With a certain amount of longitudinal traction on an artery, between its attachments, the internal diastolic pressure may be just sufficient to counterbalance this, so that there is no longitudinal tension, except that of internal strain, till the systolic rise comes; the latter would then cause lengthening and bending of the artery. Greater longitudinal traction than could be counterbalanced by the diastolic pressure is necessary to prevent bending in a relaxed artery when the systolic rise comes; the artery must be already kept stretched between its attachments to an extent as great as would result from the systolic rise of pressure. In other words if an artery is to be kept straight when internal pressure is put on, the tube must be already stretched (by external traction) as much as the internal pressure would lengthen the empty tube.

An artery stretched and bent by internal pressure gradually becomes straightened as the external pressure is raised; this is strikingly evident when an artery is examined in the compression tube in the usual way, the artery becomes shortened and straightened as the internal pressure becomes counterbalanced by external pressure.

The elongation of an empty artery which occurs with active contraction of its muscular coat is quite a different matter from the transverse and longitudinal expansion simultaneously caused by internal pressure.

When external pressure is applied so as to counterbalance the internal diastolic pressure the artery must pull on its attachments between the pulse-beats, the "passive" tube freed from internal pressure being longitudinally stretched so as to cover the required distance. The systolic rise of pressure must then have relatively little—or at least less—effect in causing elongation. The tube is already stretched by external longitudinal traction, and the rise of internal pressure may not be more, or much more, than would extend the artery to this length.

But if the artery is not stretched between its attachments and the diastolic pressure is counterbalanced by external pressure, the passive tube will elongate much more at the systolic rise. In pathological conditions arteries are often not in a state of tension between their attachments, but are greatly elongated and tortuous under the influence of the internal pressure. Removal of the latter influence by a counterbalancing external pressure causes marked shortening—in arteries that are not changed structurally in such a way as to be incapable of shortening considerably—with much elongation of the passive tube during the systolic rise; in this case the systolic elongation is not masked by existing longitudinal traction, and volume change due to elongation plays an unusually large part in the genesis of the oscillations.

Martin describes the occurrence of maximum oscillation at sub-diastolic pressures when the artery was insufficiently stretched, the mid-point of a long series of approximately maximal oscillations being taken as the maximal oscillation index; he offers no explanation of this occurrence. From our own experiments we deduce that maximal oscillation at an unusually low level may be due, in part at least, to the part played by elongation of the loose artery, large volume changes from this cause coming at a relatively early stage; it does not follow that such low level should be sub-diastolic.

In experiments by one of us (J. A. MacW.[16]) on the elongation of arteries by successive rises of internal pressure or by weights, it was found that contracted arteries gave increasing elongations up to a certain point, and relaxed arteries gave large elongations at several rises from zero, the second being often as large as, or even larger than the first. So it is evident that when external pressure is applied, elongations of large size must occur, in an artery unstretched or insufficiently stretched by traction at its ends, before the diastolic pressure is counterbalanced, *i.e.*, at sub-diastolic external pressures.

We have not in our experiments seen *maximal* oscillations at so low a level as to be actually sub-diastolic, though such might have been assumed if one relied solely on the readings from the minimum manometer on the proximal side of the artery. But in such cases direct inspection showed obvious flattening of the artery, and this made it plain that the external pressure must have exceeded the internal pressure in the artery, the latter being clearly lower than that measured by the proximal manometer; in such cases the reading of the distal manometer revealed the presence of a considerable gradient in the diastolic pressure, being decidedly below the reading of the proximal manometer. It is to be noted that Martin used an ordinary Hg. manometer to measure the internal pressure and apparently did not measure such pressure on the proximal and distal aspects of the artery.

Volume changes due to elongation must evidently have little or no effect, in the case of forms of apparatus other than the armlet which apply local pressure to a very limited area of the artery (*e.g.*, Oliver's hæmadynamometer, &c.). But these forms have many other causes of variation and fallacy associated with their working.

The decline in the oscillation magnitude from the maximal phase.

A sudden declension in the oscillation magnitude from the maximal or approximately maximal phase is an important feature in many tracings, and supplies the Recklinghausen-Erlanger index of diastolic pressure. We find that this declension is related to the cessation of the distortion of the circular tube by the external pressure. (Fig. 15 and 16.) But the absence or dubiousness of this feature constitutes a very serious difficulty in utilising this method, and one that has been widely felt. Such is the case

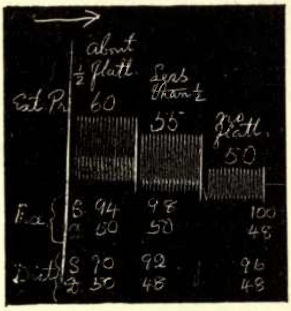


Fig. 15. Carotid, ox. The maximal oscillation occurs with half-flattening, about 10 mm. above the internal diastolic pressure. After the abrupt decline in oscillation magnitude the external pressure is close to the internal diastolic pressure (50 mm.).

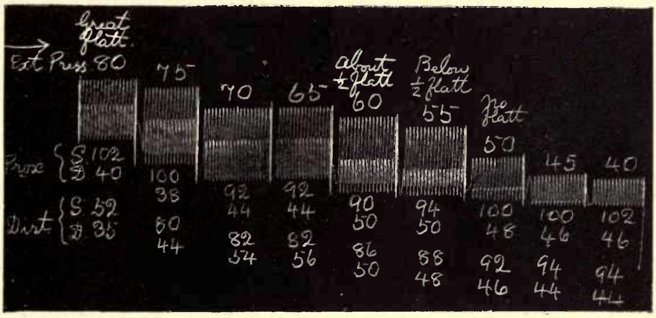


Fig. 16. Carotid, ox (relaxed). Maximum oscillation continues over a range of about 20 mm. (55 to 75 mm. external pressure). After an abrupt decline from maximum oscillation the external pressure (50 mm.) is slightly above the internal diastolic. The appearance of flattening of the artery is noted.

both with an experimental schema and with the armlet as applied clinically. In regard to the former, see Fig. 17, in which the change is seen to be a gradual one ; and no point can be fixed upon as affording an index of any kind. Such a condition is too familiar in clinical records to need illustration here. Experimentally, we have found such in arteries of very different types (*a*) relatively inelastic (Fig. 18), (*b*) contracted and resistant (Fig. 17), and (*c*) highly distensible relaxed vessels (Fig. 19).

There are various possible causes that may be stated in this connection.

The question of the volume changes due to elongation at each pulse-beat—commonly ignored in this connection—is important. If the conditions are such that elongation contributes largely to the total volume change and at a stage when the external pressure is sub-diastolic, such would tend to obscure the sharpness of the alteration determined by the beginning (or ending) of flattening of the tube.

In the case of a non-distensible tube, where the volume oscillations are due to various degrees of flattening between the beats, there would naturally be no very sharp and striking change at any phase, but rather a progressive alteration in size. (Fig. 18.) The beginning of the flattening would of course be nearer the diastolic pressure than the subsequent phases.

In a tube showing virtually only changes in length at the pulse-beats there would be a graduation in the volume changes at different external pressures—no sudden point of alteration.

With an artery relatively inelastic,* but not absolutely so, the conditions are complex. There are many possibilities, according to the degrees in which the volume changes are contributed to by changes in length, flattening of the tube or change from the diastolic to the zero position, the last named obviously depending on the extent to which the artery is distended by the diastolic pressure before the external pressure is applied.

Again, the character of the arterial wall comes in question—as to whether it is not only relatively inelastic as regards distensibility, but offers, or does not offer, marked resistance to flattening. In the latter instance there might be a sudden and marked alteration in the oscillation values at the point where the slight volume changes dependent on the alterations of the little distended circular tube from the diastolic to the zero position are suddenly augmented by the relatively large displacements associated with flattening of an easily compressible tube.

In a very distensible artery there will be relatively large oscillations, as the external pressure is raised before any flattening occurs ; the amplitude of the oscillation up to that point is indeed a measure of the distensibility of an artery, showing the extent to which it is distended by the diastolic pressure within it.

If the arterial wall offers much resistance to flattening and the increments or decrements of external pressure are small, the latter may be insufficient

---

* We mean by this term vessels of defective distensibility that are relatively little affected in transverse diameter by the blood-pressure.

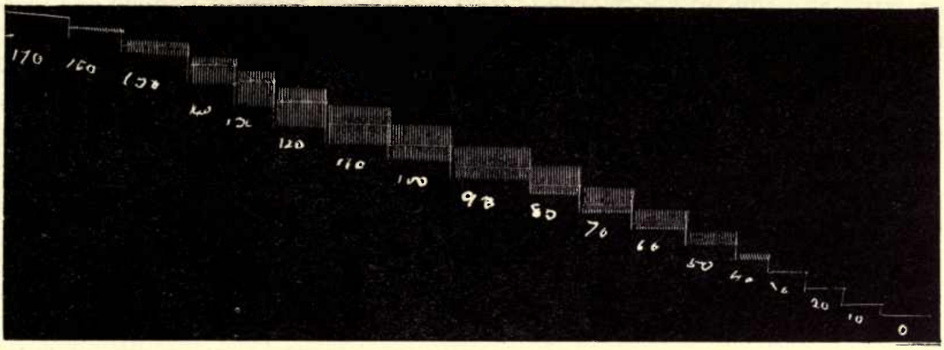


Fig. 17. Carotid, ox, contracted. A series of oscillations is seen, showing approximately maximal size over a considerable range of external pressures (marked below the tracing), with no point of sudden alteration in oscillation magnitude.

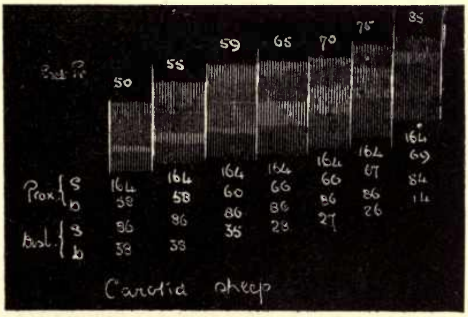


Fig. 18. In this experiment different degrees of flattening were produced in a practically non-distensible artery by rises of external pressure; the first phase (50 mm. external pressure) was attended by slight flattening, which increased in amount as the external pressure was raised. The gradual character of the changes in oscillation magnitude is evident. The lowering of the distal diastolic pressures, under the influence of the raised external pressure, is gradual in this case.

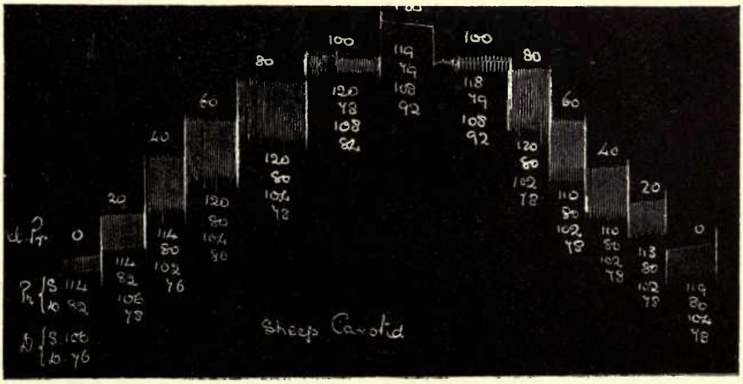


Fig. 19. The change in oscillation magnitude at different external pressures is a gradual one. No fall in the distal pressures is seen. This artery is in the relaxed state.

to cause any sudden and marked alteration in the series of volume changes, at the beginning of the process of flattening, the increment (or decrement) being insufficient to effect the change between the zero and the half-flattened positions, but only to carry it to an intermediate phase, involving a more gradual modification in amplitude.

Again, if the artery, subjected to external pressure, is unequally resistant along its course the necessary degree of flattening may be more or less gradually developed along its length.

Erlanger experimenting with tubes of peritoneal membrane associated the persistence of approximately maximal oscillation over a considerable range of extra-vascular pressure with the indistensible character of such tubes; and Janeway had noted a similar persistence in cases with sclerosed arteries or high blood-pressure.

In our experiments we have obtained a great extension of the period of practically maximal oscillation not only in non-distensible arteries (not constant in them) but also in highly distensible relaxed arteries. (Fig. 16.)

It is to be borne in mind that in obtaining oscillations from a limb by means of the armlet the conditions are by no means wholly identical with those present when a single artery is tested; in the limb the various arteries of different sizes and with different pressures and phases of maximum oscillation contribute in varying degrees to the total volume changes recorded by the apparatus.

Relation of maximum oscillation to the mean pressure.

The phase of maximum oscillation has no necessary or constant relation to the mean pressure within the artery. Under certain conditions there may be a rough correspondence between the mean pressure and the external pressure needed to elicit the maximum oscillation. But as a rule this is not the case. Neither the lowest level at which the oscillation is approximately maximal nor the mid-point of that period is a guide to mean pressure, though the latter is much nearer it than the former.

Relation of our results to the view at present accepted.

Our findings in regard to the mechanism of maximum oscillation are subversive of the view at present accepted.* According to that view the oscillations, largest when sufficient external pressure has been applied to neutralise the internal diastolic pressure and bring the vessel into the zero position, decline with raising or lowering of the external pressure from the optimum level. In the former case the external pressure becoming higher than the diastolic pressure tends, as Howell puts it, to overcome the stiffness of the arterial wall; the pulse wave then has an excess of pressure on the outside to overcome, and this is believed to involve a diminution in the oscillation volume, the movement of the arterial wall being less extensive in proportion to the excess of pressure on the outside, &c. On the other hand, with a falling external pressure only partially neutralising the diastolic pressure the lessening of the volume of the circular tube by the external pressure between the beats is insufficient to allow of the maximum range of systolic expansion; hence lessened excursions. But there is nothing here to explain the sudden decline from the maximum which often occurs and serves as the Recklinghausen-Erlanger index; in accordance with the known elastic properties of the arterial wall the decline ought to be a gradual one, depending on gradual alterations in the amount of expansion of the circular tube, such as are found experimentally when an artery is tested with definite increments or decrements of internal pressure.

---

* Many years ago Roy and Adami thought that a pulse wave of 30 mm. Hg. would produce the greatest change in the cubic contents of a portion of artery if at each pulse-beat the artery is alternately collapsed and opened out. They regarded the external pressure necessary to cause collapse of a radial artery, after excision, as being so small as to be safely negligible in the present connection.

Erlanger from direct observation of a rubber tube subjected to external pressure concluded that the maximum oscillation occurred when the relations of external and internal pressure were such that with each pulse wave the tube opened out to almost its full extent and at the end of diastole the walls just met.

According to our view the maximal oscillation only occurs when the artery is flattened between the pulse beats to a very considerable extent, *e.g.*, to half-flattening in an easily distensible tube, to complete or nearly complete flattening in a non-distensible one.

A higher external pressure causes diminished oscillation, by producing excessive flattening in a distensible artery and opposing too much resistance to systolic expansion. A lowered external pressure fails to cause any distortion of the circular tube between the beats; the systolic expansion is represented by increased distension of that tube and is sub-maximal. Often the change between the latter form of expansion and that compounded of such expansion and the opening up of a partially flattened tube is sharply marked and in our view constitutes the real basis of the Recklinghausen-Erlanger index.

But according to this interpretation the index ought not to be the usual one of taking the lowest level at which oscillation is maximal, but the level at which the markedly diminished excursions are first obtained; at this level the external pressure balances, more or less exactly, the internal diastolic, but does not exceed it sufficiently to cause distortion of the circular tube. In many of our experiments we have found this index to approach more closely to the actual diastolic pressures in the artery.

PART II.

THE AUSCULTATORY OR AUDITORY METHOD.

The auscultatory method of estimating blood-pressure proposed by Korotkoff[13] of St. Petersburg in 1905 has received comparatively little attention in this country—much less than in Germany.

Oliver[21] has described the method and devised a convenient tambour for use instead of a stethoscope.

As far as systolic estimation is concerned, all observers who have worked with this method seem to be pretty well agreed that it yields accurate indications; most observers find it more precise than the ordinary tactile method, though Gibson thinks that it cannot replace the latter.

In regard to diastolic pressure there is much uncertainty as to the indications yielded by this method. There are conflicting views as to which phase is to be regarded as the diastolic index. Thus Ettinger[6] regards the disappearance of all sounds when the armlet pressure is gradually lowered as corresponding to the minimal or diastolic pressure, while Fischer[7] believes that the latter is indicated by a change in the character of the sound (from clear to dull) some distance above the point of disappearance.

Oliver, while disposed to regard the lower limit of the sound as the diastolic index, says that there is not the same assurance on this point as in regard to the systolic index.

Lauder Brunton[2] says that the diastolic pressure may correspond to the level of a rising external pressure at which the sound appears loudly—the point where the sound increases being generally sharply marked—to disappear or at least become much feebler at a higher level; or on the other hand, that the true diastolic pressure may correspond with the loudest intensity of the sound. He remarks that experiments on animals or on a schema are needed to determine what relation the sudden increase of the sound on raising the external pressure bears to the diastolic pressure.

There is not, as far as we are aware, an investigation, under precise experimental conditions, of the auscultatory manifestations in relation with:

(*a*) accurately measured internal pressures (systolic and diastolic), taken on both the proximal and the distal side of the artery;

(*b*) direct observation of the behaviour of the arterial walls; and

(*c*) the varying degrees of oscillation in arterial volume (maximal pulsation, &c.).

Character of the sounds.

Between the upper and the lower limits of the sound production very marked variations in character and intensity are recognisable, and these show considerable differences in various circulatory conditions.

Ettinger described five phases during the lowering of the external pressure from above the obliteration point.

(1) The beginning of the sound in the form of a clear-cut sound occurring in the systolic phase, and serving as an index of systolic pressure, beginning with the passage of the first waves of blood through the artery under the armlet.

(2) A murmur of variable duration replacing the first sound.

(3) A clear sound, replacing the murmur.

(4) A transformation of the clear sound into a dull one, this change sometimes being sharply defined, at other times more gradual.

(5) Disappearance of sound.

Kryloff had previously given an account of the first three phases only. Gittings'[9] experience agreed with that of Ettinger.

Oliver describes four successive phases between the appearance and disappearance of the sound or throb, characterised by (1) sharpness, (2) murmurishness, (3) loudness, and (4) dullness. We find that an essentially similar series of sounds can be studied on an experimental schema.

Views as to the production of the sounds.

Great importance has been attached in this connection to what occurs in the artery below the seat of compression by Korotkoff and other observers. According to Korotkoff the lower portion of the brachial artery is relaxed* while the artery higher up is obliterated by the armlet, and when the first blood-waves come through (on lowering the armlet pressure) the sudden stretching of the artery lower down causes the production of sounds.

Kryloff† describes the first sound as the loudest, and puts this down to the smallness of the lumen in the artery under the armlet at this phase, and the consequent rapidity of the blood-current through it; this he looks upon as favouring a sudden stretching of the walls of the vessel below the armlet.

Ettinger considers the vibration to be more pronounced in the third phase and ascribes this to the larger volume of blood passing under the armlet, though with diminished rapidity, at this period.

Ehret regards the suddenness of the distension, and not the amplitude of the pulse-wave, as essentially affecting the intensity of the sounds. The speedy diminution of the sounds below the armlet is attributed to the less complete emptying of the artery.

To the suggestion that the sounds are really transmitted heart sounds, Kryloff opposed the consideration that all sounds disappear when the armlet pressure is lowered beyond a certain point.

Gittings favours the view that the sudden stretching of the relaxed vessel wall is the cause of the first sound. He also attaches much importance to the size and accessibility of the artery, being able to hear the sound only in exceptional instances and only for a short time over the radial or ulnar artery when the armlet was applied to the forearm. He also regards the resonating character of the armlet as a very important factor, finding that with simple compression by an Esmarch bandage the sounds are not as a rule audible.

Oliver thinks that sound is developed when the external pressure falls below the obliteration point from jets of blood being projected through a narrowed lumen into comparatively empty vessels, their impact against the relaxed walls being audible as a throb. He ascribes the variations in the quality of the throb to different amounts of blood in the relatively collapsed arteries, the varying calibre of the lumen compressed, and variations in the rapidity of the current.

Experiments with a circulatory schema.

In order to study the auscultatory phenomena and their relationships with internal pressures, oscillation of the arterial walls, &c., we have employed an arrangement similar to that described with regard to the maximum oscillation method. The rotating tap already mentioned was always used in these experiments to give the pulsatile flow; in this way the danger of confusion from sounds produced by a pump or the valves of a syringe, &c., was avoided.

Distally to the compression tube and quite close to it a piece of relaxed carotid (sheep) was often interposed and the auditory tambour or phonendoscope applied over it. In other cases the sounds were listened for over the glass tube emerging through the rubber cork at the distal end of the compression tube. The sheep's carotid was most commonly used in the compression tube; the horse's metacarpal and the carotids of the ox and horse being also tried. The former two were found to be the most suitable, especially the first.

---

* The term "relaxed" here presumably means an undistended condition of the artery, not an inactive condition of the arterial-muscle—the strict meaning of the word "relaxed."

† Quoted in Gittings' paper (Arch. of internal Medicine, 1912, vi, 196). We have not been able to see Kryloff's original communication.

With an artery (*e.g.*, carotid of sheep) in the compression tube under accurately known conditions of internal and external pressure we have correlated (*a*) the visible changes (alterations in form, vibration, &c.), in the vessel with (*b*) the sound production in different circumstances, while making simultaneous observations of (*c*) the pulsatory volume oscillation (by graphic records) and (*d*) of the occurrence of thrill, &c.

On gradually raising the external pressure, so as to cause progressive diminutions in the size of the artery from the original distension by the diastolic pressure to the zero position, no sounds are audible ; during this period the volume oscillations are gradually augmenting, but are still markedly short of the maximal size. It is only when the external pressure is further raised so as to cause some visible flattening of the circular tube in the diastolic intervals that a sound occurs with each pulse-beat (lower limit). At this point the volume oscillations are still far from maximal. Progressive augmentation of the external pressure leads to more extensive flattening and increased loudness of the sound, then the development of a murmur, the substitution of a single sound for the murmur, and finally the disappearance of this sound (upper limit). The phases of the maximum intensity of the sound or murmur are associated with extensive flattening, with very obvious vibrations of the arterial walls (often with a sensation of thrill on palpation) and large, it may be maximal, volume oscillations. The extinction of the sound is seen to coincide with a condition of complete flattening and obliteration, present even during systole, and attended by a great diminution of the volume oscillations.

On lowering the pressure from above the obliteration point the same series of changes in reversed order presents itself. The sound begins as soon as a certain amount is forced through the compressed area at each systole, this being attended by a more or less marked increase of volume oscillation—the Erlanger systolic index. The lower limit of the sound is found to coincide with the phase where the external pressure has been lowered to such a point that it just fails to cause any obvious effect in distorting the circular form of the tube in the diastolic intervals. The plan of following the changes from above downwards is to be preferred in the application of the auditory method, for in this way it is commonly possible to follow the sounds downwards to a lower level of the falling external pressure, than when one listens for the beginning of the sound with a rising external pressure.

It is quite clear that the sound production at its lower limit occurs when the external pressure exceeds the internal diastolic pressure by the amount, generally very small, required to cause slight flattening, an amount decidedly less than is needed to produce the more extensive distortion associated with maximum oscillation, with the associated murmur, thrill, &c. (Fig. 20.)

For example, with proximal pressures of 100 mm. systolic and 64 diastolic and distal pressures of 80 mm. systolic and 60 diastolic, the sound was heard distinctly while the external pressure was at 64 mm., but was not audible when the external pressure had been lowered to 62.

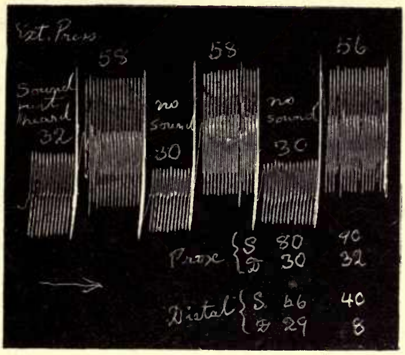


Fig. 20. The maximum oscillation, attended by a loud murmur, occurred with an external pressure much (16–18 mm.) above the internal diastolic pressure as measured manometrically and indicated accurately by the disappearance of the sound. External pressures marked above the tracing.

The evidence available from various sources renders it certain that the mid-point of the period of approximately maximal oscillation does not afford any correct indication of the internal diastolic pressure. It is as a rule decidedly too high ; in very many cases the over-estimate is an extensive one. The auscultatory index (lower limit of the sound) is always lower and corresponds more nearly with the sudden decline in oscillation magnitude, when such occurs in a sufficiently marked and characteristic form to yield reliable indications.

The auditory diastolic index comes decidedly below the level of external pressure at which marked disturbance of the distal pressure—in relation to the proximal pressure—occurs as already described when dealing with the maximal oscillation. The absence of this complication renders it possible in a schema to correlate the relations of sound and the intravascular pressures more accurately.

Production of the sounds.

As has already been stated great importance, in regard to the production of the sound, has been attached by observers to the behaviour of the brachial artery below the compressed area—the sudden distension of a more or less lax artery. But we find that on gradually raising the external pressure the sound begins when the artery is only slightly flattened, so that there is no appreciable interference with the flow through it and no change in the systolic or diastolic pressures in the artery beyond. Hence there is at this time nothing to cause imperfect filling of a lax artery beyond, with the possibility of sudden distension at the systolic—beyond the ordinary systolic distension which takes place in any artery with no external pressure applied, and in which no sound is produced. The same holds good in regard to the sound production near its lower limit, when the external pressure is gradually lowered.

When using an artery in the compression tube in the way described, with no piece of artery on the distal side, but the phonendoscope or tambour applied over the glass tube issuing from the artery in the compression tube, we find that the sounds are perfectly well developed and characteristic—a fact which controverts the idea of the essential importance of the artery distally to the compressed area.

Experiments with rubber tubes of the ordinary kinds we used were found to be unsatisfactory ; with special thin-walled tubing the result might be different. Under the influence of different heights of external pressure in the compression tube or armlet, the tube showed flattening to various extents between the systoles with blowing sounds, &c., but not the characteristic sound production ; the volume changes much resembled those in an extremely resistant and non-distensile artery, and the changes in the internal pressures (distal especially) were similar. Under such conditions a length (20 cm., &c.) of sheep's carotid (relaxed) which readily gave the characteristic sounds when tested in the compression tube, was placed distally to the compression tube and close to it. The pressure and flow in this distal artery (*i.e.*, the artery below the seat of compression) was markedly affected by the action of certain heights of external pressure on the rubber tube (obliteration, half-flattening, &c., in the latter), but no sound was audible at any part of it. Sudden variations in the distension of this artery due to changes in the degree of compression of the rubber tube were not accompanied by the characteristic sounds.

It is indeed not easy to conceive how such sound could be produced from the further distension of an elastic artery of circular form any more than by the normal systolic expansion of a very distensile artery (relaxed, &c.) with no external pressure applied.

Evidence as to the sound production is also obtainable from examination (in man) of the effects of compression of a very limited area of the artery, instead of the extended compression by the armlet. We find that the sound is quite audible though relatively feeble when suitable pressure is applied to the brachial with the finger. The feebleness of the sound in this case is opposed to the current view of the sound production. For if the condition of the artery on the distal side ("empty" or lax, undistended, &c.), is the essential point, the sound ought to be well developed, the condition of the distal artery being capable of being affected in the same way by compression higher up, whether it is by the armlet or the finger—the blood-stream reaching the distal artery is similarly affected in both cases. The great influence of the length of artery subjected to compression points to the importance of that area as the seat of sound production.

With reference to the possible influence of the air in the armlet as a resonating medium, to which much importance has been attached by Gittings, we find that the sounds are quite well marked when the artery in the compression tube is not in relation with an air cushion at all, the whole space around the artery and the tubes connected with the compression tube being entirely filled with liquid. The loud murmur attended by very obvious vibration of the arterial walls, occurs with a suitable external pressure under these circumstances in characteristic fashion.

As regards the timing of the sounds we find that the position of the latter in the cycle of changes at each pulse-beat may under certain circumstances vary considerably, sometimes coming early in the systolic phase, sometimes much later—towards the end of this phase, &c.

In addition to a study of the phenomena observable during the succession of systolic and diastolic phases recurring at the rates of pulsation (60, 80, &c., per min.) we have tried the effects of maintaining these phases for longer periods, the stream being more or less suddenly turned on and kept flowing for some time, then turned off with varying degrees of suddenness; in this way it can be tested whether the sounds are due to a sudden rise or a sudden fall of internal pressure setting up vibration in the arterial walls, &c.; various levels of external pressure are maintained during these observations.

It was found that, with a suitable external pressure, the sound is generally produced when the pressure is turned on, *i.e.*, at the systolic phase, though with certain arrangements in the experimental schema we noted the production of sound in the diastolic phase.

Under certain conditions sound is not only audible when the pressure is turned on, but persists as a continuous murmur as long as the stream is kept flowing through the artery, while a certain level of external pressure is kept up; lowering of the external pressure causes the murmur to be replaced by a single sound when the internal pressure is turned on. With too low or too high an external pressure no sound is heard. The murmur varies markedly in pitch, being of higher pitch with a higher external pressure. Accompanying the murmur there is a remarkable amount of thrill which can be felt with the hand applied to the compression tube or to one of the tubes leading to or from the artery. Active vibration of the arterial walls is very obvious on direct inspection, and is plainly evident in the column of fluid in a vertical glass tube connected with the stream distally to the compression tube. The rate of oscillation of the fluid in the vertical tube alters strikingly with the variations in the pitch of the murmur; this is determined by changes in the height of the external pressure within certain limits.

These facts recall the vibratory or purring sensation that can often be recognised with the hand applied over some of the larger arteries in cases of aortic regurgitation.

Indication of arterial distensibility.

As the declension of the sound serves as a guide to the beginning of appreciable flattening it is evident that an indication of the distensibility of an artery is afforded by the extent of the oscillation elicited in presence of a fair systolic wave—by raising the external pressure to the level at which the auditory diastolic index is obtained. The possible oscillation range up to that point varies with the extent to which the arterial volume has been enlarged by the internal diastolic pressure before the external pressure was applied. Of course the amount of the distending force at each beat as indicated by the pulse-pressure is an essential factor in this connection ; a pulse-pressure of higher value than that of the original diastolic pressure will cause, under clinical conditions, expansion beyond the diastolic position. The amount of this will vary according as the artery yields much or little to the further increase of pressure ; this will be influenced by the height of the diastolic pressure and the amount of distension produced by it, for an artery already much distended by a high diastolic pressure will yield proportionately little to a further (systolic) rise of pressure.

We have made observations of this kind both under clinical conditions and with excised arteries.

A modification of the compression tube method.

The advantages of the compression tube method are obviously great, the behaviour of the artery under different external pressures being open to direct inspection, while the volume changes are recorded graphically, the sounds heard, the internal pressures measured, &c. But there is one point of notable difference from the conditions present when an armlet is applied to a human limb in the usual way, inasmuch as in the compression tube the ends of the artery are tied on rigid (glass) tubes, which keep them open even when the rest of the vessel is more or less completely closed by a high external pressure. Of course in a limb the artery outside the area of compression, proximal and distal to the armlet, remains open, but there is not the same rigidity at the junction of the compressed and the non-compressed (circular) portions of the tube. As it is plain from direct inspection of the artery in the compression tube that at certain phases the movements of the arterial walls are specially extensive and vigorous near the ends it is very possible that an important influence on sound production may be exercised by those portions of the vessel under the special conditions in which they are placed.

A method of eliminating this possibly disturbing influence of the glass tubes is to use an artery which has been prepared in a special way. Its distal and proximal ends where tied on the glass tubes are treated, for a distance of about a centimetre, with formalin, and thus rendered much more resistant than the rest of the vessel, with the result that when the external pressure is gradually raised the main part of the artery becomes flattened, while the terminal portions still remain circular, the latter corresponding in this respect to the artery below (or above) the armlet in ordinary blood-pressure estimations in man. The movements (flattening and recovery) of the artery in the compression tube are in this way removed some distance from the ends of the glass tubes and uncomplicated by the possible influence of the physical conditions associated with the direct attachment of the moving arterial walls to the rigid tube.

When tested in this way the auditory method yielded very definite results. The sounds, though weaker and differing somewhat in character from those heard by the first described method, presented the essential features of well-defined upper and lower limits with an intervening murmur phase, &c. The upper limit served well as a systolic index, and the lower quite as well as a diastolic index, yielding definite indications of the actual internal pressures as measured manometrically.

When an arrangement of this sort was used a modification was sometimes made by adding a length of artery (12-14 cm., &c.) on the distal side of the compression tube, to represent the continuation of the human artery distally to the armlet. The added length of artery had previously been tested in the compression tube in the usual way and found to give the characteristic sounds in very marked fashion. This distally-placed artery underwent marked changes when the artery in the compression tube was subjected to sufficient external pressure. But either no sound, or no intensification of the sound already found to be produced in the compression tube, could be heard, when one listened over the early part of the distally-placed artery.

There was not the slightest indication of sound production distally to the compression tube, though the artery placed there was undergoing changes in internal pressure very similar to those present in a human artery distally to the armlet. Sounds heard at the beginning of this artery were much less pronounced than those heard over the short glass tube connecting the artery placed within the compression tube with the distally-placed length of artery ; sound heard at the beginning of the latter was evidently transmitted from the artery in the compression tube and rapidly faded away on listening a little further along the vessel in the distal direction.

The indisputable fact that closure of the artery on the distal side of the armlet and some little distance away abolishes the sounds has been construed in favour of the current view of sound production. Ehret, for example, contends that in this condition the changes in the artery actually compressed by the armlet are much the same as usual, while those in the distal portion of the artery distally are much modified ; he regards this as proving that the seat of the normal sound production is in the distal portion.

Our own observations upon arteries (examined in the compression tube in the way described) have shown that when the artery is closed on the distal side the changes in the part subjected to external compression are influenced notably and in a fashion similar to the distal portion, though perhaps not so extensively.

Further, we attach great importance to the presence of an active flow through the vessel in the normal process of sound production ; the absence of flow depending on distal closure of the artery would naturally be accompanied by an upset of the conditions in which the ordinary sound is present.

The current reasoning as to the production of the sounds in the early part of the artery lying distally to the compressed area postulates the occurrence of extensive changes in this part, depending on the influence of compression of the vessel by the armlet higher up. The distal artery is assumed to be more or less collapsed, and then the sudden distension by the pulse-wave is the reputed cause of the sound. In regard to this it is necessary to bear in mind that the conditions are very different near the lower limit of sound production as compared with the higher phases (*i.e.*, at higher external pressures in the armlet). When the compressing pressure is gradually lowered from the obliteration level, the first systolic jets of blood forcing through the compressed area enter a relatively undistended distal artery, the pressure in which is low, being the residual pressure in the vessels of the part of the limb peripheral to the occluding armlet. The exact amount of such residual pressure will vary according as the armlet has been slowly or quickly inflated to the obliteration point; in the former case the venous return will be obstructed for a considerable time before the arterial inflow is arrested, and so the vessels in that area become congested. With rapid inflation the residual pressure is less. But in any case there is such pressure present in the distal portion of the brachial artery as to keep the tube in the circular form, unless in presence of some distorting force such as traction upon its ends or attachments sufficient to cause flattening in spite of the influence of the internal pressure. It is difficult to believe that the sound is produced by the sudden distension of an uncompressed artery which is in the circular form; such does not occur in a relaxed artery undergoing change of this sort under the influence of the pulse-pressure, apart from the presence of external pressure. If such is the genesis of the sound in question why should an ordinary relaxed artery in a limb or elsewhere not give similar sounds when suddenly distended by a good systolic rise? Resonance by the air in the armlet can hardly affect sound produced in the distal artery, whatever it might do in regard to sounds arising in the length of artery compressed by the armlet. (See also p. 190.)

Again, if sudden distension of the distal artery can be a source of sound, is there any good ground for excluding the artery compressed by the armlet from sound production, especially when rapid changes from the flattened to the circular form and *vice versa* come into play—the changes that are essentially associated with sound production in an artery enclosed in the compression tube as already described.

Current views as to sound production in the distal artery based on the assumption that this part is lax and undistended obviously fail to afford any feasible explanation of sound production at and near its lower limit. For at that phase it is quite clear from our experimental evidence that the pressures (systolic and diastolic) in the distal artery are not influenced by the compressing pressure higher up; there is no obstruction or interference with the flow through the compressed area, and the distal artery is quite in its normal condition as regards distension, &c., instead of being lax or undistended or relatively empty and specially susceptible of sudden distension by the systolic wave, as is involved in the current hypothesis.

Experiments on excised arteries by the armlet method.

We have performed such experiments in addition to those with the compression tube as already described. With a rising external pressure the flattening of the artery begins near the distal end and the movements are most active there while the external pressure is raised to a considerable distance; near the systolic (obliteration) level, on the other hand, the movements are most pronounced near the proximal end, or confined to that end. In the intermediate period there is active movement (flattening and recovery) along the whole length of the vessel, at least in the case of an artery presenting no great differences in resistance along its length.

We have embedded a length of artery (*e.g.*, 20 cm.) in a portion of an animal's limb (ox, &c.) so as to lie in relation to the bone much as the brachial artery is in relation to the humerus in man. The armlet was then applied in the usual way. The artery was introduced into the circuit of the schema, the compression tube being omitted; the arrangement of the proximal and distal manometers was the same as before. Auscultation was used near the emergence of the artery from the area compressed by the armlet.

The sounds heard with this arrangement were much less loud than with the preceding method of experiment, and somewhat different in character, but the upper and lower limits of the sound were found to correspond very closely with the systolic and diastolic levels as already described.

Definition of the diastolic index in man.

During gradual lowering of the armlet pressure from the region (intermediate between systolic and diastolic pressures) where the sound is very loud, there comes at a certain level a sudden and marked alteration in the sound, which becomes diminished in intensity and duller in character. This alteration may be succeeded (1) by a continued persistence of the altered sound through an extensive further lowering (*e.g.*, 20-30 mm.) of the armlet pressure, or (2) by a speedy or almost immediate extinction of the sound. The alteration in question is, as we have evidence to show, the index of diastolic pressure. In other words the diastolic index is a sudden declension in the sound, which may or may not be speedily followed by its extinction. Such declension occurs when the armlet pressure is no longer sufficient to cause distortion of the arterial tube from the circular form.

In very many healthy persons, in a majority of the young adults (students) examined in a *quiet* room, the sound was found to persist as in

---

In a young adult in fair health, with no sign of aortic regurgitation, a persistent sound was audible over the brachial when there was no armlet pressure at all. The diastolic index above-mentioned was distinctly got at about 60 mm.

(1) to excessively low levels, retaining the character of a dull thud, quite distinct though weak, down to such levels of armlet pressure as 28, 32 mm., &c. Here the lower limit of the sound is obviously no indication of diastolic pressure, but is very far below the latter. The diastolic index is afforded by the marked change from a sharp to a duller and less loud sound occurring at a much higher level (*e.g.*, 60 mm., &c.).

From the results obtained in such cases it is clear that there may be conditions in the human subject under which sound production may persist after the armlet pressure has fallen below the amount necessary to cause any flattening of the circular tube, but still suffices to diminish to some extent the calibre of the artery from the diastolic size, the arterial wall being brought into a position intermediate between the diastolic and zero positions. Here the segment of vessel included under the armlet, though still circular, is diminished in size as compared with the artery on the proximal and distal sides of the area compressed by the armlet.

In the great majority of cases examined in hospital wards where absolute quiet was not attainable, and also in many healthy and diseased persons examined in a quiet room, the results were such as are indicated under (2), closely resembling those obtained with the experimental schema. (In the latter absolute quiet was not usually attainable.)

We have correlated the data obtained by the auditory method with those supplied by an extended series of observations by the oscillation method on normal and pathological subjects carried out by workers in this laboratory. The results of these observations will be published later.

Limitations and sources of fallacy in the auditory method.

These are in our experience relatively few and unimportant.

1. We have found experimentally that very large and extremely distensible tubes like the relaxed and softened carotid of the ox and horse and stiff thick-walled strongly contracted carotids of the same animals do not give satisfactory results by this method. But the conditions in such experiments are very extreme and far removed from what may possibly be found in man, and we have not found any evidence of similar failure to obtain definite results in thickened and stiffened arteries under clinical conditions.

2. The auditory method is not applicable in many cases of aortic regurgitation on account of the continued presence—apart from the application of external pressure by the armlet—of the well-known sound.

3. We have seen abundant evidence (experimental and clinical) that a very defective rush of fluid through the artery under examination can impair the validity of the auscultatory criteria. Such may result from various causes such as the following :—(*a*) Congestion and stagnation of blood in the limb distally to the armlet as a result of keeping on the constriction

too long. This also causes the artery distal to the armlet to be much more filled up with blood (*i.e.*, at higher internal pressure) than in the ordinary procedure. (*b*) Excessively small calibre from thickening, constriction, &c., of the artery examined or of its continuation. (*c*) An extremely low pulse-pressure, due to very small cardiac output (feeble heart, very excessive pulse-rate, &c.) with relaxed peripheral vessels, &c.

4. While the brachial artery is excellently adapted for this method, application of the armlet to the forearm gives unsatisfactory results. The range of sound heard over the radial artery is defective, being shortened both above and below, *i.e.*, the systolic index is too low and the diastolic too high. That the systolic reading is too low is shown by comparison with the tactile or the visual index. This would naturally be associated with a similar defect at the lower limit, the sound being cut down too soon. That such is the case is corroborated by the fact that the diastolic reading thus obtained is higher in the forearm than in the arm—an obvious error in the former.

5. The possibility of conduction of the sound along a bone occasionally comes into question both as regards the systolic and the diastolic index. On this point one of us (G.S.M.) and Mr. J. R. Murray have obtained evidence which will be stated elsewhere.

It need only be stated here that with the routine procedure recommended below there is no danger of error in this way.

6. Improper adjustment of the auditory tambour, &c., might possibly lead to inaccuracy, but not when the tambour is properly situated with no appreciable pressure.

In all the conditions mentioned the sound declines too soon when the external pressure is being lowered, thus making the reading of diastolic pressure too high. But the same causes lead to the appearance of the systolic sound—when the pressure is lowered from that causing complete obliteration —being delayed, and so underestimating the actual systolic pressure.

Such an undue lowering of the upper limit of the sound is readily recognisable by using the tactile systolic index simultaneously, and this affords a most important indication of the unreliability of the sudden declension as an index of diastolic pressure.

We adopt and recommend as a routine procedure the simultaneous determination of (1) the reappearance of the pulse by the ordinary tactile method, and (2) the auditory systolic index, as a method of verifying the correct arrangement of the auditory apparatus (tambour, &c.) and its applicability to the conditions present in any particular case.

In doubtful cases, when dealing with arteries that are abnormally thick or contracted, offering considerable resistance on palpation when the internal blood-pressure is excluded, the method of local compression as recommended in a former paper, is very useful in checking the systolic readings, being equally applicable to the tactile and the auditory estimations. (*Heart,* IV, 279.)

We have not in our experimental schema found the sound persisting at so low a level as to underestimate the actual diastolic pressure in the vessel. When there is a considerable pressure gradient in the stream, the diastolic index may sometimes be got below the reading of the proximal minimum manometer, but never below the average between the proximal and distal manometers, and obviously not below the actual diastolic pressure in the artery; the distinct flattening occurring in the latter shows that the extra-vascular pressure is somewhat in excess of the intra-vascular diastolic pressure—by the amount necessary to cause the distortion in the tube.

But as has already been stated conditions may be present in the human limb which lead to a persistence of the sound (as tested in quiet surroundings) far below the level of diastolic pressure, the latter being indicated by a sudden weakening or dulling of the sound, not its extinction. In other conditions the extinction nearly coincides with the sudden alteration just referred to.

We have very often used Oliver's tambour for attaching over the artery on the distal aspect of the armlet; this has the advantage of leaving the hands of the observer free. Instead of this we have often used a phonendoscope or a binaural stethoscope. For conveniently graduating the application of the external pressure Oliver's screw-compressor when employed with a suitable armlet (with a rubber bag of not too large capacity) is very useful.

Advantages of the auscultatory method.

Comparing the auditory method of diastolic pressure estimation with the maximum oscillation method as represented by the best graphically recording apparatus in use (Erlanger's), the superiority of the former is conspicuous in many respects.

(1) The simplicity and quickness of the procedure are obviously very great considerations, dispensing as it does with the relatively cumbrous apparatus of smoked drum, recording tambour, &c.

(2) The greater definiteness of the index, as compared with the frequent difficulty and uncertainty of the Recklinghausen-Erlanger index.

(3) The greater constancy of the results. Apart from movements of the limb, the Erlanger record is apt to vary much, and this is not surprising in view of the complexity of the conditions which may be present and play a part in influencing the oscillations, as has already been described.

The auditory index is much less disturbed by alterations in the arterial walls (resistance, distensibility, &c.); this naturally results from the required degree of flattening of the arterial tube being very much less than in the other method, while in a vessel presenting unequal resistance along its course, change from the circular form in a comparatively short piece suffices to produce a sound, while flattening along the whole or the greater part is needed to give maximal oscillations ; numerous influences may tend to give a gradation in the development of the oscillation, and an absence of any sudden and striking change in the size of the oscillations. The greater degree of flattening approaching complete flattening necessary to give maximal oscillation in a practically non-distensible tube is an important factor, while the form of the pulse curve may also be such as to aid in increasing the excess of external pressure required. The varying influence of volume changes due to elongation does not come into question in the auditory method.

(4) The avoidance of the discomfort and disturbance (circulatory, &c.) which may be caused by the constriction of the limb when the pressure is raised well above the obliteration point to begin with and during the lowering of the pressure while the graphic record is being made.

Systolic and diastolic pressure estimations.

The estimation of diastolic pressure by the auscultatory method is a process that takes very little time and trouble and yields very definite and valuable information. The procedure is one calculated to produce less circulatory disturbance in abnormally sensitive cases than the stronger (obliterative) constriction of a comparatively large vascular area involved in systolic determination.

Moreover diastolic estimation is much less, if to any appreciable extent at all, affected by the main sources of fallacy in systolic estimation—variations in the resistance of the arterial wall, possibility of reflected waves, &c.

Even comparatively slight changes in diastolic pressure, unless dependent on alterations in the pulse-rate, are of considerable significance as indications of circulatory conditions (changes in peripheral resistance, &c.).

We have to thank Dr. J. E. Kesson for valuable assistance in the earlier experiments of this investigation.

CONCLUSIONS.

The current view, founded on Marey's principle, that maximum oscillation (or pulsation) occurs when the external pressure counterbalances the internal diastolic pressure so as to bring the artery to the size of the undistended tube is erroneous.

With a normal distensible and elastic artery maximum oscillation occurs when the external pressure is sufficient to distort the arterial tube so as to produce the condition which we have termed half-flattening—in which the shorter diameter is roughly about half that of the undistended tube. The volume of the oscillation is compounded of (*a*) the difference in capacity between the half-flattened and the circular tube, (*b*) the distension of the latter caused by the systolic wave and (*c*) such volume change as may result from longitudinal expansion at each pulse-beat. Variations in (*c*) are not adequately represented in experiments that have been made on the arteries of animals *in situ*.

With a more or less non-distensible tube volume oscillations are more or less completely due to different degrees of flattening, a higher external pressure being needed to bring out the maximum effect.

Maximum oscillation does not serve as a guide to the mean pressure within the artery ; there is no necessary or constant relation between the two.

The development and position of the maximum oscillation varies much, being readily influenced by a variety of conditions affecting one or more of the components of the volume changes, *e.g.*, such conditions as (*a*) the distensibility and flexibility of the arterial walls, (*b*) the time available between the beats, (*c*) the form of the internal pressure curve, and (*d*) the part played by elongation of the vessel at each beat.

Maximum oscillation occurs at levels of external pressure above, and often very considerably above, the actual internal diastolic pressure, the excess varying between a few mm. Hg. and 20 mm. or more.

The taking of the mid-point in the period of approximately maximal oscillation is an erroneous method of gauging internal diastolic pressure, widely varying overestimates being thus obtained.

The differentiation (during the lowering of the external pressure) of the last phase at which the oscillation is maximal (the Recklinghausen-Erlanger index) is often uncertain or impracticable. When a characteristic change in oscillation magnitude is clearly recognisable it affords a valuable index. We regard the level of external pressure just *after* the abrupt diminution has taken place as the better guide. This external pressure is just insufficient to cause any flattening.

Methods of estimating diastolic pressure by examination (palpatory or graphic) of changes occurring in the artery peripheral to the armlet (Strassburger, Masing, Sahli, Bingel) are not to be recommended, the indications being dubious and their interpretation unreliable. The same is to be said of subjective change in the sense of throb in the limb as an indication.

The sounds concerned in the auscultatory or auditory method of blood-pressure estimation (diastolic and systolic) owe their origin to vibration of the arterial wall when the normal circular form of the vessel is, in the compression area, more or less distorted by external pressure. The level of armlet pressure at which the sound suddenly declines, becoming weaker and duller, is to be taken as the index of intra-arterial diastolic pressure ; at this level the external pressure has become insufficient to cause any flattening of the circular tube.

The auditory method provides a quick and simple method of approximately estimating the diastolic pressure, more precise and easily interpreted and less disturbed by abnormal conditions than the indications (visual graphic, &c.), yielded by other methods, rendering the latter unnecessary.

The estimation of diastolic pressure by this method should be combined (as a routine practice) with the use of the auditory method for systolic estimation, checked by the ordinary tactile method—in order to confirm the validity of the auditory method as applied in any particular case. This combination we strongly recommend ; also the use of local compression as an aid in doubtful cases (with resistant arterial walls, &c.), in the estimation of the systolic pressure.

Diastolic pressure estimation by the auditory method is not only as simple in application as the systolic estimation, but is comparatively little, if at all, influenced by many of the complications as regards local conditions, &c., which may in some cases introduce serious fallacy into systolic estimations ; it also causes less disturbance (circulatory, &c.), in very sensitive subjects, much less constriction of the limb being needed.

The pulse-pressure range as determined by the auditory method is much more extensive in many pathological conditions than is indicated by the ordinarily accepted ratios.

Changes in diastolic pressure of relatively small amount, unless dependent on an altered pulse-rate, are of much significance as indications of circulatory conditions.

BIBLIOGRAPHY.

[1] BINGEL. München. med. Wochenschr., 1906, LIII, 1246.

[2] BRUNTON. Brit. med. Journ., 1910, II, 1389.

[3] EHRET. München. med. Wochenschr., 1909, LVI, 606 and 959.

[4] EHRET. München. med. Wochenschr., 1911, LVIII, 243.

[5] ERLANGER. Johns Hopkins Hosp. Rep., 1904, XII, 53.

[6] ETTINGER. Wien. klin. Wochenschr., 1907, XX, 992.

[7] FISCHER. Zeitschr. f. diätet. u. physik. Therap., 1909, XII, 389.

[8] GIBSON. Proc. roy. Soc. Edin., 1907-8, XXVIII, 343.

[9] GITTINGS. Arch. of internal Medicine, 1912, VI, 196.

[10] GUMPRECHT. Zeitschr. f. klin. Med., 1900, XXXIX, 377.

[11] HILL AND BARNARD. Proc. physiol. Soc., p. IV, Journ. of Physiol., 1898, XXIII, ; *Lancet*, 1898, I, 282.

[12] HOWELL AND BRUSH. Boston Med. and Surg. Journ., 1901, CXLV, 146.

[13] JANEWAY. "Clin. Study of Blood Pressure," New York, 1910, 89 ; New York Bull. of Med. Sci., 1901, I, 165.

[14] KOROTKOFF. Mittheilungen der kaiserl. Milit-Mediz. Akad. z. St. Petersburg, 1905, XI, 365.

[15] MACKENZIE. "Diseases of the Heart," London, 1910, 99.

[16] MACWILLIAM. Proc. roy. Soc., 1902, LXX, 109.

[17] MAREY. Travaux du Laboratoire, 1880, IV, 253, Ibid., 1876, II, 316.

[18] MARTIN. Brit. med. Journ., 1905, I, 865.

[19] MASING. Deutsch. Archiv. f. klin. Med., 1902, LXXIV, 253.

[20] MOSSO. Arch. Ital. de Biol., 1895, XXIII, 177.

[21] OLIVER. Quart. Journ. of exper. Physiol., 1911, IV, 45.

[22] PACHON. Brit. med. Journ., 1910, II, 1765.

[23] RECKLINGHAUSEN. Archiv. f. exper. Pathol. u. Pharmakol., 1906, LV, 375.

[24] ROY AND ADAMI. *Practitioner*, 1890, XLV, 32.

[25] SAHLI. "Lehrbuch. d. klin. Untersuchungsmethoden," 2nd edit., 1899, 140.

[26] STANTON. Univ. of Pennsylvania med. Bull., 1903, XV, 466.

[27] STRASSBURGER. Zeitschr. f. klin. Med., 1904, LIV, 373.

[28] TSCHLENOFF. Zeitschr. f. diätet. u. physik. Therap., 1898, I, 328.

DIASTOLIC BLOOD-PRESSURE ESTIMATIONS BY THE AUSCULTATORY AND OSCILLATION METHODS.

By G. SPENCER MELVIN and J. R. MURRAY. (From the Physiological Laboratory, University of Aberdeen.) (With nine figures in the text.)

(*Received for publication* 14*th February* 1914.)

THOUGH the auscultatory method of blood-pressure estimation, suggested by Korotkoff (16), has been tried by various observers in different countries, especially in Germany and America, and though the sounds heard are remarkably well defined and easy to recognise, there has been nothing like a general—nothing, indeed, beyond a very limited—application of the method, as regards diastolic pressure, to clinical or physiological purposes. In this country Oliver (22, 23) has advocated the method, and has devised very serviceable apparatus for its application. With regard to the estimation of diastolic pressure—the chief advantage claimed for the auditory method—much uncertainty has been felt, and sharply conflicting evidence has been advanced in regard to the absolutely essential question as to what phase in the series of auditory phenomena is to be taken as a true indication of diastolic or minimum pressure within the artery. Further, the evidence as to the relation between the auditory phenomena and the oscillation results, obtained graphically by accurate methods, has been conflicting, and has not hitherto been regarded as sufficiently convincing. Again, there are no sufficient data as to the normal average and range of variation of the diastolic pressure, estimated with due precautions by the auditory method, in an adequate series of healthy adults and children to serve as a rational basis for the study of diastolic pressure by this method in diseased states.

The chief objects of the present investigation have been (1) to establish a reliable index of diastolic pressure by making an accurate comparison between (*a*) the auditory phenomena, (*b*) the tactile indications, and (*c*) the volume oscillations as studied by the Erlanger sphygmomanometer, in view of the results obtained in a recent investigation with an experimental schema in this laboratory, (*a*) in a series of healthy young adults (59), (*b*) in a series of children with healthy circulations; (2) to obtain data to warrant a conclusion as to (*a*) the normal average diastolic pressure, (*b*) the range of its variation in healthy persons, and (*c*) the average value and range of the variation of pulse-pressure in normal conditions.

METHOD.

The subject was seated—the usual precautions as to the absence of muscular contraction in the arm under examination being observed—the armlet (12 cm. broad) approximately at the level of the heart.[1] The procedure was first to test the efficiency of the auditory method, as applied in each individual, by a comparison of the auditory and tactile systolic indices, the former being found to be at least as high as the latter, and generally higher by some millimetres. (In any case where the auditory index was below the tactile, and this was not remediable by attention to the tambour, the auditory method was recognised as untrustworthy as applied in that particular case—in regard to both systolic and diastolic pressures.) The armlet pressure was then gradually lowered, and the auditory phenomena were examined while an Erlanger tracing was made. The armlet pressure was raised again, and the sequence of events noted in the reversed order as regards the limits of the phases of sound production, the comparison of the tactile and auditory systolic indices, etc. Care was taken to avoid congestion of the arm when the auditory estimation was made. The pulse rate was also recorded, as being a factor of importance in gauging the significance of different heights of diastolic pressure, especially as indications of peripheral resistance.

In using the Erlanger sphygmomanometer the method of continuous escapement, though much more expeditious and often less disturbing to the subject, was abandoned as often giving tracings which offered greater difficulty in interpretation than the slower and more laborious method of interrupted escapement. The latter plan has been recommended by Erlanger, Janeway, and others. Even with this method much difficulty was often experienced. We have usually lowered the armlet pressure by 10 mm. stages, though we sometimes tried 5 mm. A drawback to the latter is not only the longer time consumed, but also the diminished sharpness in the alteration in the oscillation which is being looked for, so that in doubtful cases the difficulty in deciding the index may be increased.

OSCILLATORY AND AUDITORY INDICATIONS OF SYSTOLIC PRESSURE

The systolic index which Erlanger (4, 5), following Recklinghausen (24), employs (depending on a sudden increase in the oscillation and a separation of the limbs as the armlet pressure is being lowered) has proved unsatisfactory in many cases, being unreadable or giving indications at variance with those yielded by the tactile and auditory methods, the oscillation index being in some cases much higher and in other cases decidedly lower than the auditory index, corroborated by the tactile index.

---

[1] An ordinary armlet in conjunction with a mercury manometer was used, an Oliver tambour (phonendoscope) strapped on the arm being employed to examine the sounds. This tambour is a very delicate one, provided (as Oliver has pointed out) that it is thoroughly air-tight.

Not infrequently the oscillations are developed in such a way as to make it impossible to fix upon any phase as the systolic index. Many observers have found difficulty in regard to this index. In a recent investigation (on healthy subjects) Weysse and Lutz were unable to make a reading in 37 per cent. of their tracings. Such failure of the oscillatory systolic index is of relatively little importance, as the auditory and tactile indices are available for the purpose. It is in regard to the diastolic pressure that the main importance of the oscillatory method is based.

Erlanger has described the oscillations as increasing in size during the lowering of the armlet pressure, until the diastolic level is reached; with Festerling (7) he has made this the basis of a proposed method of obtaining continuous records of blood-pressure in man. The same principle had been already applied by Erlanger and by Eyster (9). The rationale is that with an armlet pressure between systolic and diastolic a rise of arterial pressure (involving an approach of the intra-arterial minimum pressure towards the extra-arterial pressure) would result in an increase in the amplitude of the oscillations, and vice versâ.

In our own experience we have often observed a progressive increase up to the point where marked lessening begins, but such a feature is not present in the majority of our tracings. Often the oscillation continues at the maximal level for a considerable period before the fall begins; often there is a gradual but quite appreciable diminution to an "approximate maximum," followed immediately by a marked lessening or in some instances by a series of progressive reductions with no predominant phase of sudden diminution, or with such a phase coming later in the series. The absence of a progressive increase up to the beginning of the phase of diminution is very common in our observations.

OSCILLATORY AND AUDITORY INDICATIONS OF DIASTOLIC PRESSURE.

Interpretation of Oscillation Tracings.

The index generally employed in the interpretation of oscillation tracings is, of course, the one recommended by Recklinghausen, Erlanger, Janeway (14), and others,—the last level of falling armlet pressure at which the oscillations are maximal. In view of the results of a recent investigation with an experimental model in this laboratory, and other considerations, we have preferred as the diastolic index the average of the armlet pressures just before and just after a sudden and marked decline in the oscillation from the maximal or approximately maximal size. It has been shown in a former paper (MacWilliam and Melvin (18)) that when the external pressure falls just below what is necessary to cause flattening of the arterial tube between the pulse beats, the volume oscillation undergoes a marked diminution. This is in opposition to the observation (on rubber tubes) of Erlanger (4) that the oscillation ceases to be maximal when the external pressure is not sufficient to bring the sides of the tubes into contact between the beats, and the widely accepted view of Howell that the maximal oscillation occurs when the external pressure suffices to balance the internal diastolic pressure and bring the artery to the size of the undistended circular tube with no pressure in its interior but kept patent by the rigidity of its walls. MacWilliam and Melvin have emphasised the consideration that the behaviour of the oscillation may be influenced by alterations in the part played by changes in the length of the artery at each pulse beat in contributing to the volume oscillations, the changes in the artery being in turn capable of being influenced by variations in the degree to which the vessel is kept stretched between its attachments.

When the external pressure is lowered by 10 mm. stages it is evident that the point in question may lie anywhere within the 10 mm. Consequently, we take the average as the safest plan on the whole, though not regarding it as an exact indication in any particular instance. Thus with the marked diminution of the oscillation occurring when the armlet pressure is lowered from 70 to 60 mm., we take the reading as 65 mm., though the actual point of change may be nearer 70 or nearer 60.

When there is an abrupt decline from an oscillation that is absolutely maximal no difficulty in interpretation arises (figs. 1, 2, 4.) In many instances, however, there is a decline from the actual maximum to a phase which is appreciably smaller, but is still large and separated by no abrupt or extensive alteration from the maximum. Such a phase we have, for the sake of convenience, termed "approximately maximal," as distinguished from the actual maximum. The approximate maximum is often followed by a pretty abrupt diminution in the oscillation, much more extensive than the change from the actual to the approximate maximum (fig. 3). Here the question arises as to whether the former or the latter change is to be regarded as the diastolic indication. Difficulty may in some instances be felt as to how far down the very gradually diminishing series the oscillation may be regarded as "approximately maximal," and whether the slight diminution from the actual maximum is or is not sufficient to constitute the diastolic index, when a more sudden and extensive diminution comes later (fig. 9). Upon such variations depends the difficulty of fixing the index in some instances.

The Auditory Diastolic Index.

We use the division of the auditory phenomena into the five phases proposed by Ettinger (8), and now generally adopted—(1) sharp clear sound, (2) muffled and murmurish, (3) loud and clear, (4) dull, (5) abolition of sound.

There has been much conflict as to what constitutes the index. Korotkoff described the "end-tone" as the index. Among succeeding observers Ettinger (8), Ehret (2), Gittings (12), Goodman and A. A.

Howell (13), Schrumpf and Zabel (26), and others have used the lower limit or abolition of the sound (5th phase).[1]

On the other hand, the adoption of the beginning of the 4th phase has been supported by Fischer (11), Lang and Manswetowa (17), Warfield (30), Taussig and Cook (29), and Weysse and Lutz (31).

Oliver (22) at first regarded the lower limit of sound (5th phase) as the index, but has in a very recent communication slightly modified his position, as stated below.

We regard the dulling and weakening of the sound at the beginning of the 4th phase as the diastolic index, on grounds that have been stated elsewhere.

DURATION OF THE FOURTH PHASE.

As regards the duration of the 4th phase, there has been some difference of opinion; but all previous observers have made it short or relatively short. Goodman and A. A. Howell state 6 mm. Warfield puts it, for normal pressures, at 4 to 10 mm., occasionally not more than 2 to 4 mm., but with high pressures never less than 8 mm., and sometimes as high as 16 mm. Weysse and Lutz made it at most 25 mm. Oliver evidently regards the change in the sound and the lower limit as being so close that the latter serves sufficiently well for clinical purposes, i.e. the duration of the 4th phase is, from this point of view, negligible. In the diagram which he gives (fig. 3, p. 91), the two points are represented as being near each other. He thinks it probable "that the ordinarily accepted diastolic pressure—as indicated by the optimum oscillation point of an indicator—should be placed higher on the scale" (than the lower limit), "namely, while reading with the rising pressure, at the point when the throb changes its quality from a dull muffled tone to a clear loud note . . . but really all we require for clinical purposes is the definite localisation of the minimum and maximum pressures, which is so sharp at the lower and upper limits of the range of throb that all who run may read, and the personal equation is nil."

In the present series very different values have been obtained:—(1) In one class of cases a duration of only a few mm.; (2) in another a duration extending to greater amounts, and often rising to 30 to 50 mm. We have not found that (2) was confined to normal, or associated with low pressures, as Fischer thought, but was frequently present with high pressures. On the other hand, (2) was commonly observed in individuals with normal or rather low pressures. In the tabular statement of fourteen instances where there was an extended 4th phase, it is seen that the average diastolic pressure is not substantially lowered, as compared with the average of the whole series of 59 young adults. It is clear from our results that the persistence of the 4th phase may often be so long that to take the lower limit as the diastolic index would in many cases lead to hopelessly erroneous results. It is evident that the question as to whether the beginning of the 4th phase or the 5th phase constitutes the index is an absolutely fundamental one. The prolonged 4th phase we found in the majority of healthy young adults examined in a perfectly quiet room, but only in a small number of persons of more advanced age examined in hospital wards. This may account for much of the divergence in the records of the subject.

---

[1] This view is also held by W. H. Howell (Text-book of Physiology, 1913, 5th edit., 495).

Table I.—Table of Fourteen Cases showing prolonged Fourth Phase.

No.	Pulse rate.	Aud. syst.	Aud. diast.	Lower limit.	Diff. bet. diast. and lower limit.	Pulse pressure.	Range bet. syst. and lower limit.
2	70	102	80	29	51	22	73
5	99	130	70	24	46	60	106
14	104	106	50	27	23	56	79
17	84	116	62	30	32	54	86
18	66	112	62	20	42	50	92
19	78	106	56	24	32	50	82
23	72	118	65	20	45	53	98
33	110	118	65	24	41	53	94
37	87	105	65	10	55	40	95
38	80	114	52	14	38	62	100
39	72	105	61	30	31	44	75
41	60	92	54	30	24	38	62
54	60	112	64	30	34	48	82
58	90	127	65	22	43	62	105
Averages	81	111·5	62	23·8	38·3	49·5	87·8

It is to be noted that the average duration of the 4th phase is vastly greater than has been suggested by former observers, and that there is no constant association with variations in pulse rates, systolic pressures, or pulse-pressures. The range between systolic pressure and the lower limit of the sound is an enormous one.

Relation of Oscillatory and Auditory Indices.

We find that there may be variation in regard to the phase in the oscillation record which corresponds with the auditory diastolic index. In no case does the latter correspond with the maximum oscillation; our results are quite uniform on that point.

The auditory index is commonly associated with a marked decline in the oscillation following (*a*) maximal oscillation (figs. 1 and 4), or (*b*) a period of "approximately maximal" oscillation, i.e. one which is not maximal but has undergone some gradual diminution without any sudden or marked alteration (figs. 3, 5, and 6). In some instances the auditory index may come between (*a*) and (*b*) (fig. 7).

It sometimes, though rarely, happens that the auditory index may (*c*) not correspond with any notable feature in the tracing, or (*d*) correspond to a marked diminution in the oscillation, the most marked and sudden diminution seen in the tracing, but coming at a much later phase than (*a*) or (*b*).

It is to be noted that the auditory index may agree with the first change from the maximal oscillation even in cases where an approximate maximum is present (fig. 4).

DISCORDANCE BETWEEN OSCILLATORY AND AUDITORY INDICATIONS.

In cases of marked discordance between the oscillation and the auditory indices, which is to be relied on? We prefer the auditory to the oscillation reading on various grounds.

(1) There is often discordance between the systolic indices also, and there the tactile index is available as a test; it always confirms the auditory rather than the oscillation index. The variability of the oscillation indications in regard to systolic pressure and their frequent untrustworthiness are very significant in the present connexion, suggesting unreliability at the diastolic level also.

(2) The results with an experimental model showed the much greater reliability of the auditory method in estimating minimum pressure as measured by valved manometers. Experiments by MacWilliam and Melvin have also shown the constancy of the diastolic indications in estimating local variations in diastolic pressure (induced by gravity) in man.

(3) The complexity of the conditions on which the oscillation magnitude depends and their liability to variation under different conditions such as may be present in the limb under examination.

(4) The definiteness of the auditory change (taken as the diastolic index) and its association under experimental conditions with a change from an external pressure sufficient to cause distortion of the circular tube to one insufficient to cause any flattening, i.e. an external pressure equal to the internal diastolic pressure. The evidence already stated makes it certain that the level of diastolic pressure coincides not with the lower limit of the sound, but in each particular case with a definite point at a higher level in the series of auditory phenomena.[1]

RESULTS.

Comparatively little difficulty was experienced in making the readings, the chief one being in deciding whether a slight change from the actual to

---

[1] Note added March 14, 1914:—(5) Direct experimental proof from animals, as stated in Proc. Phys. Soc. of this date. See also Brit. Med. Journ., March 28, 1914.

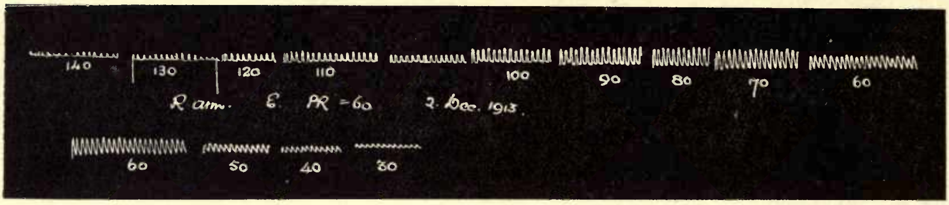


FIG. 1.—Agreement of OD and AD. OD taken at change from actual maximal = 65 AD = 64. Oscillation diminishes suddenly from maximal, and there is no phase of approximate maximal. Last actual maximal = 70. Lower limit of sound = 30. Fourth phase = 34.

The following abbreviations are used with reference to the tracings and tables in this paper :—

AD. = auditory diastolic.
OD. = oscillatory diastolic by our index.
AS. = auditory systolic.
OS. = oscillatory systolic (Recklinghausen-Erlanger).
TS. = tactile systolic.
PR. = pulse rate.
Aud. = auditory.
Erl. = diastolic reading according to Erlanger's index.
Tact. = tactile.
Osc. = oscillatory index as employed by us.
T-Osc. = tactile-oscillatory.

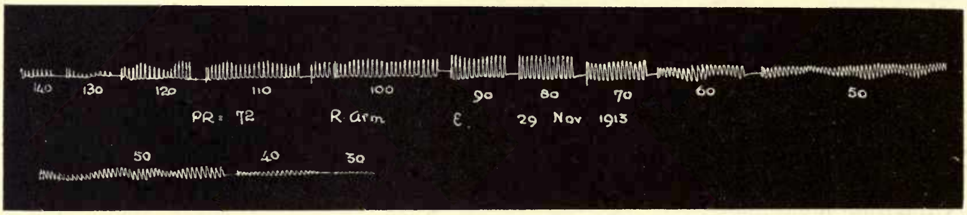


FIG. 2.—Discrepancy between OD and AD. OD = 75, taking change from actual maximal, or 80 taking last oscillation that is maximal. Even in change from phase following maximal phase OD would be 65—still much higher than AD, but it is clear that the change from the maximal is the one that must be taken. AD = 54. Lower limit of sound = 35, corresponds to nothing definite in tracing. Fourth phase amounts to 19.

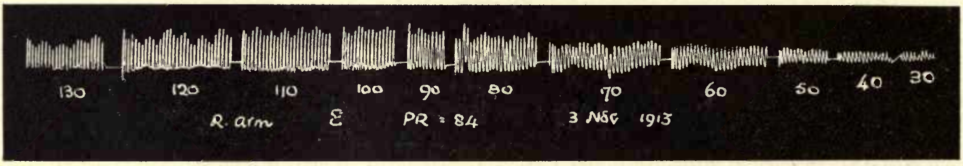


FIG. 3.—Agreement of AD and OD. OD = 75, taking change from approximate not actual maximal. AD = 73. Lower limit = 52. Fourth phase = 21. Last phase that is maximal = 90.

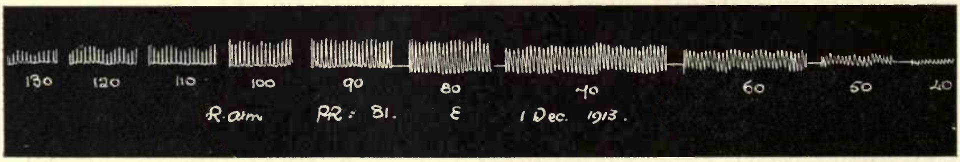


FIG. 4.—Agreement of OD and AD if OD taken as diminution from actual maximal = 75. AD = 75. If the oscillation at 70 be regarded as "approximately maximal," OD would be = 65. The diminution from 70 to 60 is relatively greater than that from 80 to 70. Lower limit of sound = 52. Fourth phase = 23.

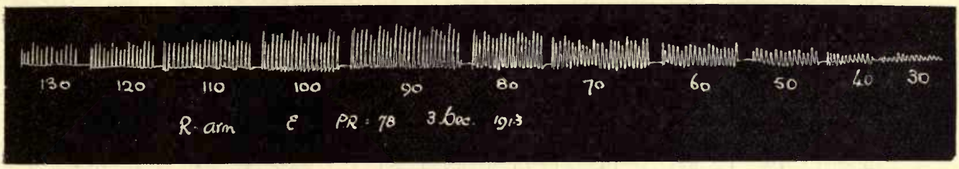


Fig. 5.—Agreement between OD and AD. OD = 75, taking diminution from approximate not actual maximal. AD = 73. Lower limit of sound = 52. Fourth phase = 21. Last oscillation of maximal size is at 90.

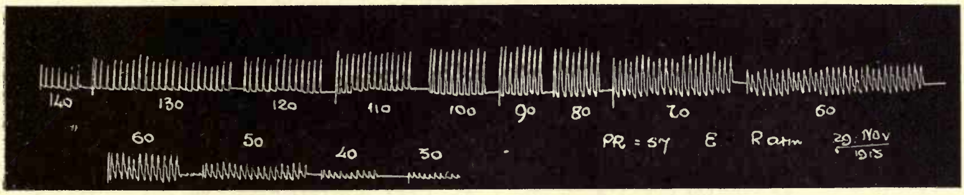


Fig. 6.—OD, taking diminution from approximate maximal = 65. AD = 67. If change from actual maximal taken, OD would = 75. Last phase of maximal oscillation = 80. Lower limit of sound = 40. Fourth phase = 25.

In regard to the AS index, the conditions were peculiar in this subject. It was found impossible to abolish the sound even by high armlet pressures, whilst TS was 106. There was a decided change (sudden increase) in the sound at 112 mm., which we take as the AS index. The persistence of the sound at higher levels is probably due to conduction along the humerus.

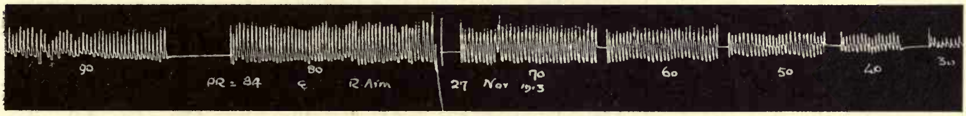


Fig. 7.—OD = 65, taking diminution from actual maximal. AD = 60. The next diminution, from 60 to 50, is more extensive—this would make OD = 55. Lower limit of sound = 50. Fourth phase = 10.

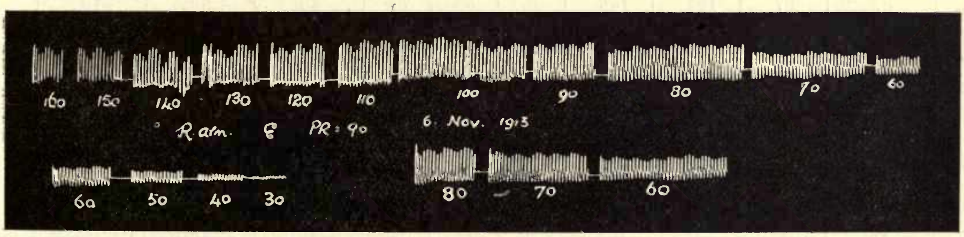


Fig. 8.—Discrepancy between AD and OD. OD = 75, taking diminution from approximate maximal. AD = 65. Lower limit of sound = 22. Fourth phase = 43. Oscillation continues nearly maximal for a long period. 120 to 80.

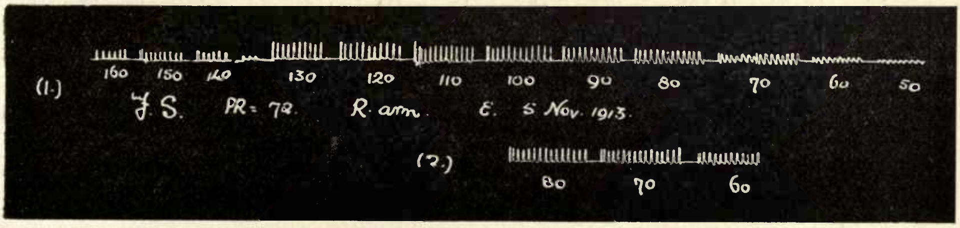


Fig. 9.—OD = 75. Agreement with AD, taking change from approximate maximal. AD = 72.

TABLE II.—TABLE OF RESULTS OBTAINED FROM HEALTHY YOUNG ADULTS.

No.	Pulse rate.	Systolic.		Diastolic.			Pulse pressure aud.	Pulse pressure T-osc.	Lower limit.
		Tact.	Aud.	Erl.	Osc.	Aud.			
1	78	118	120	70	65	65	55	53	45
2	70	94	102	70	65	80	22	29	29
3	60	104	108	70	65	61	47	39	38
4	72	100	102	80	75	59	43	25	42
5	99	128	130	80	75	70	60	53	24
6	84	118	124	90	75	51	73	43	33
7	129	124	126	90	75	72	54	49	52
8	78	104	104	70	65	69	35	39	60
9	80	118	122	90	85	80	42	33	59
10	80	128	128	90	85	77	51	45	37
11	92	108	108	90	85	74	34	23	51
12	96	98	98	70	65	69	29	33	60
13	100	126	126	80	65	63	63	61	38
14	104	100	106	80	75	50	56	25	27
15	80	118	118	90	75	76	42	43	67
16	88	98	100	70	55	57	43	43	52
17	84	104	116	70	65	62	54	39	30
18	66	112	112	70	65	62	50	47	20
19	78	106	106	80	55	56	50	51	24
20	84	132	134	90	75	72	62	57	60
21	90	100	102	80	65	62	40	35	48
22	100	106	110	70	65	68	42	41	40
23	72	114	118	90	75	65	53	39	20
24	90	114	116	80	75	76	40	39	44
25	84	98	104	80	65	69	35	33	56
26	72	112	118	80	75	75	43	37	62
27	72	102	102	70	65	71	31	37	40
28	108	126	128	90	75	64	64	51	34
29	80	98	102	80	55	55	47	43	38
30	86	98	98	70	65	64	34	33	54
31	102	114	116	70	65	65	51	49	38
32	66	106	106	60	55	66	40	51	48
33	110	100	118	80	65	65	53	35	24
34	68	100	104	70	65	55	49	35	36
35	84	112	116	70	65	61	55	47	32
36	78	101	102	80	65	66	36	36	58
37	87	104	105	70	65	65	40	39	10
38	80	112	114	70	55	52	62	57	14
39	72	103	105	80	75	61	44	28	30
40	78	115	116	80	75	74	42	40	45
41	60	92	92	70	35	54	38	57	30
42	90	108	116	70	65	54	62	43	54
43	80	108	110	70	65	64	46	43	44
44	60	96	96	70	65	70	26	31	56
45	90	128	135	90	85	82	53	43	70
46	72	104	104	70	65	76	28	39	63
47	75	98	98	70	65	62	36	33	50
48	50	101	108	70	55	59	49	46	52
49	72	112	112	80	75	54	58	37	35
50	57	106	112	80	65	67	45	41	40
51	84	100	106	80	65	65	41	35	46
52	100	116	116	70	65	64	52	51	40
53	81	104	104	80	75	75	29	29	52
54	60	107	112	70	65	64	48	42	30
55	84	108	115	110	75	76	39	33	52
56	78	112	114	90	75	73	41	37	52
57	72	114	128	?90	75	72	56	39	35
58	90	126	127	110	75	65	62	51	22
59	84	104	104	70	65	60	44	39	50
Averages	80·1	108·7	111·8	78·3	68	65·7	46	40·7	42·2

Series here dealt with is not identical with the one referred to in a former paper. Many of the higher pulse-rates above seem to be due to temporary excitement.

the approximately maximal, or a much larger one following the approximate maximum should be taken as the index. The results were much less variable than was found to be the case with the experimental schema already referred to. It was found possible to make a reading in every tracing. This is in contrast with what Weysse and Lutz found in a recent investigation; they were unable to make a diastolic reading in 32 per cent. of their Erlanger tracings. These workers used the method of continuous escapement at so quick a rate (as shown by the few tracings they publish) that a fall of armlet pressure from 140 to 70 mm. occurred in the time occupied by only about 37 heart-beats, and a fall from 130 to 60 mm. about 42 heart-beats, etc.

Our results show remarkably close agreement as regards the average diastolic pressure as read by the oscillation and the auditory methods. Various points are brought out in the tracings (figs. 1 to 8). Discrepancy amounting to 10 and over between the auditory and oscillatory indications (fig. 8) occurred in nineteen instances (31 per cent.); in fourteen of these the auditory index was lower, and in five higher than the oscillatory. Sometimes the auditory index corresponded, with marked diminution in the oscillation (the most marked change occurring anywhere) coming later than the maximal or approximately maximal phases.

OBSERVATIONS ON CHILDREN.

Though there are numerous records of systolic pressure in children there seems to be little or nothing in the way of diastolic estimation; as to the normal level of diastolic pressure in children we have not been able to find any published evidence.

In view of the unsatisfactory results commonly obtained from the human forearm by the auditory method, it might be surmised that this method would probably not be applicable to the small arms of children. Such, however, has not been our experience with children down to the age of about eight years. The indications have been found to be very definite, and it is easy to obtain both systolic and diastolic readings. We check the auditory systolic by the tactile index (according to our usual routine) to establish the validity of the former by finding normal relation similar to that described for adults. A narrower armlet (e.g. 8 c.m.) is more conveniently used.

It is to be noted that the general level of systolic and diastolic pressure does not differ much from that found in young adults. This is in opposition to the view of observers who have stated the systolic pressure as decidedly lower in children, e.g. 90 mm.

The pulse-pressure in children comes out at a much lower value than in adults, and this is not always associated with the quicker pulse of children, e.g. in No. 3. An exceptionally slow pulse was noted in No. 4, with a larger pulse-pressure. The quick pulse of children would naturally tend to give a high diastolic pressure.

Subjoined are a few readings from children with no evidence of circulatory disease:—

Table III.

No.	Age.	Pulse rate.	Aud. syst.	Aud. diast.	Pulse pressure.
1	10	100	108	80	28
2	12	102	105	78	27
3	10	60	90	55	35
4	12½	50	108	65	43
5	14	84	108	78	30
6	12	84	115	80	35
7	12	84	113	77	36
8	10	92	110	86	24
9	12	100	110	70	40
10	13	106	100	70	30
11	8	104	112	75	37
12	14	88	106	68	38
Averages	11·6	87·8	107	73·5	33·5

Ratio of pulse pressure to syst. = 1 : 3, 2, and to diast. = 1 : 2, 2.

Average Level of Diastolic Pressure and Range of Variation.

Evidence as to the normal level of diastolic pressure is scanty and hard to find in the literature of the subject. In many cases no information is available as to the number of individuals examined, their ages, whether in normal health or not, etc. The statements made are very discordant, the differences no doubt depending on the various methods and indices employed, the age and condition of the subjects, etc. Erlanger is quoted by Howell (15) as putting the diastolic level at 65, and Recklinghausen at 73 mm. We have been unable to verify this reference to Erlanger's result, or to find any published statement by him as to average diastolic pressure estimated on a series of healthy persons. All we have been able to find are isolated observations in different conditions. Thus Erlanger and Hooker (6) recorded minimal pressures mostly between 80 and 100 mm. in a few subjects in the sitting or recumbent positions. More recently Erlanger refers to patients who had returned to the normal after heart-block as having diastolic pressures of 74 mm. Obviously such patients cannot be taken as good subjects for the determination of normal diastolic pressure. Oliver (21) obtained values of 90 to 100 mm. by the oscillatory, and 75 to 95 mm. by the auditory method. Fellner (10) gives an average of 96 mm. Janeway in his well-known book states tentatively a range of 65 to 110 mm. for diastolic pressure. Strassburger (28), using his palpatory method, and Sahli (25) using, like Masing (20), a sphygmographic method, assign high values to diastolic pressure, as they regard the pulse-pressure as only about one-fourth of the systolic pressure. Among recent workers by the auditory method Goodman and A. A. Howell state 85 mm., and Stone (27) 80 mm. Weysse and Lutz do not state any average, but the legends of some of their tracings mention 82, 80, and 73 as diastolic values.

From the tabular statement of the results obtained in our series of healthy young adults (p. 58), it is seen that the average diastolic pressure by the auditory method is 65·7 mm. By the oscillation method, using our index, 68·0 m., and by the Erlanger index 78·3 mm. Thus the maximum oscillation is very decidedly above the auditory index, as was also found to be, as a rule, the case with an experimental model. With reference to the latter, there was a notable similarity between the character of the curves—behaviour as regards the development and the decline of the oscillations, etc., in the case of the model and in man.

AVERAGE PULSE-PRESSURE AND RANGE OF VARIATION.

The importance of a knowledge of the pulse-pressure and the inadequacy of systolic estimations by themselves are being gradually recognised. Various estimates of pulse-pressure have naturally resulted from the varying estimates of diastolic pressure. Erroneous readings of systolic pressure, due to abnormal conditions of the vessels, have, no doubt, also been a source of fallacy in some cases.

Though the pulse-pressure has been put at 45 mm., the great majority of observers have stated much lower values. Strassburger, Sahli, Fellner, and Lauder Brunton (1) agree in stating its relation to systolic pressure as 1 : 4. Janeway has taken a similar view—pulse-pressure 25 to 40, with systolic pressure at 100 to 130. Oliver stated 25, Eichberg (by Recklinghausen's tonometer) about 30, and Fellner 29 mm. Goodman and A. A. Howell made it 40 mm., the same figure as stated by Stone. The pulse-pressure Stone finds to be 50 per cent. of the diastolic pressure; this he considers the "normal cardiac load," reckoning excess over this percentage as "overload," e.g. a pulse-pressure amounting to 71 per cent. of the diastolic pressure he regards as an overload of 21 per cent.

As we find the auditory indices decidedly more precise and reliable than the others, we rely upon the values obtained by them for systolic and diastolic pressures, with the resulting pulse-pressure. We find the average pulse-pressure by the auditory method to be 46·1 mm.,[1] which amounts to 41·2 per cent. of the average systolic and 67·7 per cent. of the average diastolic pressure.

Using the older method of comparing the tactile systolic readings (108·7 mm.) with the diastolic readings (68 mm.) obtained from our series of Erlanger tracings (by the method of interpretation which, as stated, we prefer), the pulse-pressure comes out at 40·7 mm. Using the same diastolic index (68) with the auditory index of systolic pressure (111·8) the pulse-pressure is equal to 43·8 mm.

---

[1] This corresponds pretty closely with the pulse-pressure of 45 mm. deducible from the systolic and diastolic values attributed to Erlanger by Howell.

If our tracings are interpreted by taking the diastolic index used by Erlanger along with the auditory systolic index, the pulse-pressure would average 33·5 mm.

CONCLUSIONS.

1. The auditory method, checked by comparison of the tactile and auditory systolic indices, is by far the simplest and most precise method of blood-pressure estimation, giving results that are more accurate and more easily obtained than those yielded by the oscillatory method.

2. In the series of healthy young adults there is virtual agreement between the average value of the diastolic pressure as tested by (*a*) the oscillation (68 mm.), and (*b*) the auditory method (65·7 mm.). Under (*a*) we refer to the use of our index: with the Erlanger index the average is different (78·3 mm.).

3. The auditory index of diastolic pressure is the sudden weakening and dulling of the sound (beginning of the 4th phase) during the lowering of the armlet pressure, and not the abolition of the sound (5th phase). The difference between these two phases may be very slight or may extend to 55 mm. In the latter case utterly fallacious results would be obtained by taking the lower limit of the sound as the diastolic index.

4. In 59 healthy young adults with an average age of 20·9 years, the average diastolic pressure was found to be 65·7 mm., the range of variation being between 82 and 50 mm. In about 50 per cent. of these subjects the diastolic pressure was 60 to 70 mm., in over 20 per cent. 50 to 60 mm., and in slightly under 30 per cent. 70 to 80 mm.

5. In the series the average pulse-pressure was 46 mm., the variations being between 73 and 22 mm.

6. The average pulse rate in the series was 80·1 per minute. No relation could be made out between the pulse rate and (*a*) the height of diastolic pressure, or (*b*) the lower limit of the sound.

7. In children down to the age of eight years, the auditory method was found to be easily applicable, giving an average diastolic value, at ages between eight and fourteen, of 74 mm., and an average pulse-pressure of 33 mm.

We desire to record our thanks to Professor MacWilliam for much valued advice and assistance in this investigation.

REFERENCES.

(1) BRUNTON, Brit. Med. Journ., 1910, ii. 1389.

(2) EHRET, Münch. med. Wochenschr., 1909, lvi. 606, 951.

(3) EICHBERG, Journ. Amer. Med. Assoc., 1909, li. 1000.

(4) ERLANGER, Johns Hopkins Hosp. Reports, 1904, xii. 53.

(5) ERLANGER, Amer. Journ. Physiol., xxi.; Proc. Amer. Physiol. Soc., xxiv.

(6) ERLANGER and HOOKER, Johns Hopkins Hosp. Reports, 1904, xii. 1451.

(7) ERLANGER and FESTERLING, Journ. Exper. Med., 1912, xv. 373.

(8) ETTINGER, Wiener klin. Wochenschr., 1907, xx. 992.

(9) EYSTER, Journ. Exp. Med., 1906, viii. 565.

(10) FELLNER, Deutsch. Arch. f. klin. Med., lxxxiv.

(11) FISCHER, Deutsch. med. Wochenschr., 1908, xxxiv. 1141.

(12) GITTINGS, Arch. Int. Med., 1910, vi. 196.

(13) GOODMAN and A. A. HOWELL, Amer. Journ. Med. Sciences, 1911, cxlii. 334.

(14) JANEWAY, Clinical study of blood-pressure, New York, 1910, 109.

(15) HOWELL, Text-book of Physiology, 1913, 496.

(16) KOROTKOFF, Mittheil. d. kaiserl. milit. med. Akad. zu St. Petersburg, 1905, xi. 365.

(17) LANG and MANSWETOWA, Deutsch. Arch. f. klin. Med., 1908, xciv. 441.

(18) MACWILLIAM and MELVIN, Heart, 1913–14, v.

(19) MACWILLIAM and MELVIN, Brit. Med. Journ., 1914, i.

(20) MASING, Arch. f. klin. Med., 1902, lxxiv. 253.

(21) OLIVER, Studies in blood-pressure, London, 1908, 81.

(22) OLIVER, Quart. Journ. Exper. Physiol., 1911, iv. 45.

(23) OLIVER, Practitioner, 1914, xcii. 80.

(24) RECKLINGHAUSEN, Arch. f. exp. Path. u. Pharmak., xlvi. 78, and 1906, lv. 375, 412.

(25) SAHLI, Deutsch. Arch. f. klin. Med., 1904, lxxxi. 493.

(26) SCHRUMPF and ZABEL, Münch. med. Wochenschr., 1909, lvi. 704.

(27) STONE, Journ. Amer. Med. Assoc., 1913, lxi. 1256.

(28) STRASSBURGER, Zeitschr. f. klin. Med., 1904, liv. 373.

(29) TAUSSIG and COOK, Arch. of Int. Med., 1913, xi. 542.

(30) WARFIELD, Journ. Amer. Med. Assoc., 1913, lxi. 1254.

(31) WEYSSE and LUTZ, Amer. Journ. Physiol., 1913, xxxii. 427.

Reprinted from the British Medical Journal, *March 28th, 1914.*

SYSTOLIC AND DIASTOLIC BLOOD PRESSURE ESTIMATION, WITH SPECIAL REFERENCE TO THE AUDITORY METHOD.*

BY

J. A. MacWILLIAM, M.D.,

AND

G. SPENCER MELVIN, M.D.,

(From the Physiological Laboratory.)

It is being gradually recognized that systolic pressure estimation, though valuable, gives very insufficient information regarding circulatory conditions in health and disease, and that a knowledge of the range of pressure change during the whole cardiac cycle would be of great importance in various ways.

The auditory method, employed in a certain way, offers distinct advantages in the estimation of systolic pressure, but its greatest importance lies in its relation to the estimation of diastolic pressure.

Significance of Diastolic Pressure.

The importance of a knowledge of diastolic pressure—the constant element in blood pressure, as Marey called it, in contradistinction to the variable systolic element—need hardly be enlarged upon. It is the load which the tissues of the arterial wall have to bear continuously during the life of the individual, the transitory systolic rises that constitute the pulse being superadded. The diastolic pressure is important not only with regard to the mechanical stress upon these tissues, but probably also with regard to the influence of an excessively high diastolic pressure upon their blood supply, especially in the vessels of the lower extremity, where, in the erect posture, the diastolic pressure is greatly augmented by the influence of gravity. The problem of the maintenance of an efficient capillary circulation in the walls of an elastic tube distended by a high internal pressure is an interesting one.

Diastolic pressure in the aorta is a measure of the strain which the aortic valve-flaps have to stand, and it is obvious that tear and wear resulting from this strain must be seriously augmented by a continued excess of pressure. Sir William Osler attaches much importance to the influence of high diastolic pressure, depending on excessive muscular exertion, in the causation of aortic incompetence in what is sometimes termed "athlete's heart."

---

*Read at the Medico-Chirurgical Society of Aberdeen on December 4th, 1913.

Aortic diastolic pressure constitutes the resistance to be overcome in the forcing open of the aortic valves in the early part of the systole of the left ventricle.

Diastolic pressure estimation is valuable with reference to the gauging of the peripheral resistance. *Ceteris paribus*, an increase of this resistance involves a rise of diastolic pressure and vice versa. But it is essential to bear in mind that certain other factors have to be kept clearly in view and given due weight in the interpretation of the meaning of the diastolic pressure indications. Apart from changes in peripheral resistance, the diastolic pressure may vary markedly as a result of changes in the rate of the heart beat, a quickened cardiac action tending *per se* to raise the diastolic level, as there is less time for the pressure to fall between the systolic elevations—that is, less time for blood to pass out from the arterial tube into the capillaries.

Conversely an excessively slow ventricular rhythm (for example, in heart-block, etc.) will *per se* give long intervals for the arterial pressure to fall, thus tending to lower the level of diastolic pressure considerably. This is indicated diagrammatically by the dotted lines in Fig. 1. The tendency to a lowering of the diastolic pressure in this way may of course be compensated or over-compensated by other vascular adjustments, so that a quick pulse-rate may coexist with a normal or low diastolic pressure.

The effect of such alterations in the heart's action must naturally be allowed for in appraising the significance of a change in the diastolic pressure readings.

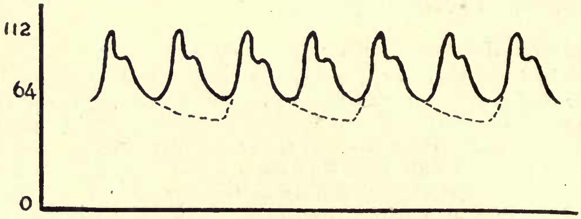


Fig. 1.—To illustrate the effect of slowing of the heart in lowering the diastolic pressure. If the heart-rate is halved the pressure has time to fall much further between the beats, as indicated by the dotted lines.

Again, a stiffening or loss of elasticity in the arterial system influences in an important way the actual height of the diastolic pressure and its relation to the height of the systolic pressure. The left ventricle pumping blood into the normally elastic arterial system of tubes produces lower systolic and higher diastolic pressures than would be present in a system of relatively inelastic or stiffened vessels. With an absolutely rigid system of tubes there would be a high systolic pressure at each pumping act, and a fall of pressure to zero between the pumping acts. It follows that the more the human arterial system approaches the condition of a rigid, as contrasted with an elastic, system of tubes the greater will be the tencency to a lowering of the diastolic pressure—with a concomitant heightening of the systolic pressure.

From these considerations it is evident that the tendency of a heightened peripheral resistance to raise the diastolic pressure may be opposed and more or less extensively modified by a stiffening of the arteries tending to lower the diastolic pressure, so that the presence of an increased peripheral resistance may be more or less completely masked, as far as a rise in diastolic pressure is concerned.

On the other hand, it is manifest that a high diastolic reading, obtained when the arterial system is stiffened and the heart-rate is not fast, must be of very great significance as an indication of increased peripheral resistance.

A change of 15 or 20 mm. in the diastolic pressure estimated under similar conditions (rest, posture, etc.) and unattended by any such alteration in the heart-rate as might in large measure account for the diastolic change, possesses a significance with regard to the behaviour of the peripheral resistance vastly greater than could be attached to a similar alteration in the reading of systolic pressure.

SIGNIFICANCE OF THE PULSE PRESSURE.

Many of the published estimates of the pulse pressure or range between the systolic and the diastolic level are no doubt vitiated by the erroneous values ascribed in a proportion of cases to the systolic pressure by taking the first readings of obliteration pressure, thus giving in certain instances a serious exaggeration of the actual systolic pressure. On the other hand, by the use of the maximum oscillation and some other methods too high estimates of diastolic pressure have often been made, while the taking of the lower limit of the sound in the auditory method as the diastolic index, as is a common practice at present, inevitably results in many instances in a wholly erroneous underestimate of the diastolic pressure.

It need hardly be said that most important information as to the state of the circulation, beyond what can be deduced from an estimation of the systolic or diastolic pressures singly, is to be obtained from a knowledge of the relation between these two—the pulse pressure. Obviously it is not merely the pressure of blood that is important, but also the velocity of the flow, determining the amount of blood which the organs receive per unit of time.

Assuming the competence of the aortic valves, it may be stated broadly that with the heart at a normal or moderate rate a defective range of pressure variation at systole and diastole—that is, a diminished pulse pressure—indicates a slowed flow of blood from the arteries into the capillaries. Thus there may be a good systolic pressure together with a lessened blood flow; this is indicated by the failure of the pressure to fall to the usual extent between the beats, the rate of the heart being of course kept in view as a factor. The converse of this rule only holds good within certain limits.

The formula that pulse pressure × pulse-rate is proportionate to the cardiac output and the velocity of the blood flow is not applicable in certain conditions (circulatory shock, etc.). Thus, in some pathological conditions there may be an extensive pulse pressure with a very defective mass movement of the blood.

The condition of aortic regurgitation, in which blood escapes from the arterial tube backwards as well as forwards, is, of course, a very special case that stands by itself.

Various observations have been made on the meaning and influence of alterations in pulse pressure.

In cases of haemorrhage it has been found by Wiggers that a progressively diminishing pulse pressure is suggestive of a continuance of the haemorrhage.

It has, of course, been long known that pulsation in the blood stream supplied to perfused organs has a very important beneficial influence upon the condition of the tissues and on the rate of perfusion.

Some ten years ago Erlanger and Hooker studied the relation of pulse pressure to renal activity; later the subject was pursued by Hooker and recently by Gesell. These investigations have produced important evidence; they concur in the finding that, as a rule, the amount of urine varies directly with the magnitude of the pulse pressure, also of the amount of urea, chlorides, etc., while in albuminuria the amount of albumin varies inversely as the magnitude of the pulse pressure. Gesell also suggests that the increased pulse pressure produced by digitalis and strophanthus may *per se* largely account for the diuresis caused by these drugs.

THE AUDITORY METHOD.

The auditory method, first suggested by Korotkoff of St. Petersburg in 1905, has so far been applied only on a very limited scale. In this country it has been recommended by Dr. George Oliver. It has been felt that there is no adequate basis of definite evidence as to the interpretation of the phenomena, at least in relation to diastolic pressure.

A prolonged investigation which we have carried out in recent years on both the experimental and clinical sides has yielded very definite results which enable us to predict for this method, applied and interpreted on lines that we have found to be reliable, a wide sphere of usefulness. From an exhaustive comparison with other methods we find that the auditory method can be made, with simple appliances and in very little time, to yield results that are unequalled, as regards range of information, precision, and reliability, by those derived from other methods, even when the latter involve time-consuming and relatively laborious procedures with more elaborate and cumbrous forms of apparatus.

The Apparatus Used.

After an extended trial of various apparatus, we use for routine examination an ordinary armlet (12 cm. broad) applied to the upper arm (not the forearm) and inflated by an ordinary ball filler, a mercury manometer (for example, Martin's form) to measure the armlet pressure, and an auditory tambour or phonendoscope (for example, Oliver's*) to auscultate the artery. This very sensitive tambour, strapped on the arm on the distal side of the armlet, has the great advantage, as compared with an ordinary binaural stethoscope or an ordinary phonendoscope, of leaving the hands of the observer free—an essential point in the application of the method as we employ it.* The tambour must be placed over the artery at the bend of the elbow close to the distal side of the armlet, and must be kept applied to the skin without exerting any appreciable pressure. It has, of course, long been a familiar fact that strong pressure applied to an artery by the end of a stethoscope causes production of sound in the vessel, the sound produced being commonly described as a murmur. Oliver remarks that it really has the character of a throb. We find that in the femoral a loud murmur is usually produced; in an artery like the radial a sharp throb or thud; in the brachial a thud, tolerably pure or with a murmurish quality. Very considerable pressure with the tambour is needed to elicit sounds in this way. With any reasonable care in the application of the tambour there is no danger of fallacy from this cause in the use of the auditory method.

---

* Supplied by Hawksley, 357, Oxford Street, London, W.

We have often used the Oliver screw compressor for inflating; it is very convenient for graduating the armlet pressure accurately by running it up and down a little near the critical point where the systolic or diastolic index is being obtained, the screw being easily turned a little forwards or backwards by one hand. The screw compressor is most conveniently used with an armlet bag of sufficiently small capacity to suit the capacity of the compressor, as is the case with the Oliver armlet, the bag going only part of the way round the limb. With a bag of larger capacity (like that of the ordinary armlet) embracing the limb completely, more than one fill of the compressor is needed, the tube to the armlet being pinched while the compressor is refilled; or, if so desired, a combination of ball filler and screw compressor may be used for rapid inflation and easy and accurate graduation of the pressure.† While the Oliver armlet gives good results upon the upper arm—care being taken that the bag is applied on the inner side over the brachial artery—we do not recommend it for application to the leg; we have found that the tactile indications obtained from the posterior tibial and dorsalis pedis arteries may sometimes be influenced by the position of the bag on the outer or inner sides of the leg. The presence of two bones with more than one large artery may evidently involve danger of fallacy when a compressing bag is used which goes only partially round the limb.

Where compactness and lightness are specially desired in the apparatus, the Oliver mercurial compressed air manometer is a convenient substitute for the ordinary mercury manometer; in a recent form the tube and scale are inclined at an angle suitable for easy reading. (The instrument should first be tested with a mercury manometer to make sure that the readings indicated on its scale are actually correct.) In its most compact and portable form the auditory apparatus may thus consist of armlet, ball filler, mercurial compressed air manometer, and auditory tambour; when the degree of compactness is not so essential, a mercury manometer (for example,

---

* We somewhat prefer the tambour attached to a separate band to the more recent form where it is held in position by a strap connected to the armlet.

† We have sometimes used, in conjunction with a ball filler alone, compression of the armlet by hand to vary the pressure up and down near the critical point.

Martin's) is to be preferred for measuring the armlet pressure.

APPLICATION OF THE AUDITORY METHOD.

In making an estimation (see Fig. 2), the armlet pressure is first raised well above systolic pressure, as indicated by the disappearance of the pulse, tested by the ordinary tactile method. When this is done, no sound is heard over the brachial artery at the elbow. The armlet pressure is then gradually lowered, and as soon as this pressure fails to keep the artery obliterated and blood begins to force its way beneath the armlet at each heart beat, a sound is heard in the form of a distinct thud. The beginning of this sound serves as the index of systolic pressure, affording a very sharp and precise indication. With a finger on the artery it is recognized that the beginning of this sound comes at least as early as the reappearance of the pulse tested by the tactile method; indeed, the former is usually a few millimetres above the latter—for example, 5 to 10 mm. The commencement of the sound is in no case below the tactile indication when the auditory method is working properly. The armlet pressure being gradually lowered, the sound becomes louder and may develop a murmurish quality, as Oliver describes it. At a lower level it diminishes in intensity, at one point rather suddenly becoming weaker, and at the same time changing in character from a clear to a duller sound. This change in intensity and character may (1) be very speedily followed by extinction of the sound, or may (2) on the other hand, be followed by persistence of the sound through a very considerable range of further lowering of the armlet pressure (for example, 20 to 30 mm., etc). The weakening and dulling of the sound we regard as the index of diastolic pressure, for reasons to be stated later, in opposition to the view that extinction of the sound constitutes the diastolic index. The lower limit of the sound is an indication which seems to be at present very widely adopted as the basis of interpretation of diastolic readings and used in the calculation of pulse pressures, etc. Quiet surroundings are, of course, necessary for the precise recognition of sound persisting below the diastolic

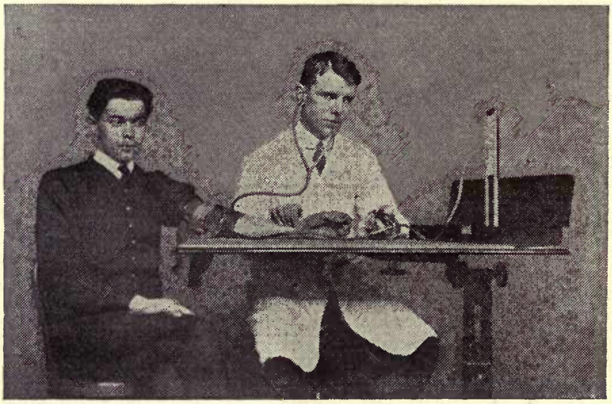


Fig. 2.

index. It is in young adults that marked persistence has, in our experience, been most frequently observed; in older persons, and in most cases examined in the wards of a general hospital, extinction of the sound has very speedily followed the occurrence of the change which constitutes the diastolic index.

The normal relation of the auditory and tactile systolic indices is of great importance; we wish to lay stress upon the concurrent estimation and comparison of these two indices as an essential part of the routine application of the auditory method of estimating systolic and diastolic blood pressures. The auditory reading should always be *at least as high* as the tactile reading; very often it is somewhat higher—a few millimetres, up to 10 mm., etc. An auditory reading lower in value than the tactile one at once impugns the accuracy of the auditory results, and shows that the conditions are such as to make the auditory indications, both systolic and diastolic, erroneous. Such conditions may be constituted by improper application of the auditory tambour over the artery, anatomical variation of the latter, etc., and may be remediable. If attention to the adjustment of the apparatus does not raise the auditory index to or above the level of the tactile index, the auditory method is to be regarded as inapplicable; we have rarely met with such a case. Abnormal lowering of the auditory as compared with the tactile index means that the former is erroneous, and there is no good ground for assuming that the alteration of the sound at a lower level of armlet pressure which constitutes the diastolic index should in these circumstances afford any valid evidence as to the height of the diastolic pressure.

By the use of the auditory method it is easy to estimate, with an accuracy not otherwise attainable, the influence of various agencies on the blood pressure—the slight variations associated with the normal respiratory movements, as well as slower periodic variations; the changes occurring in Müller's and Valsalva's experiments; the effects of voluntary muscular contraction in other limbs, the muscles of the limb embraced by the armlet being, of course, kept relaxed, etc.

Estimation of Systolic Pressure.

As far as systolic pressure is concerned, the chief advantage of the auditory method is that the sense of hearing is substituted for the somewhat more fallible tactile sense. The auditory index shows more precisely when the systolic jet of blood begins to arrive on the distal side of the armlet, being more accurate than the finger in detecting such beginning, and serving as a sharper indication of the point where the intra-arterial systolic pressure begins to overpass the external or armlet pressure. The use of the auditory method in this connexion is open to certain possibilities of fallacy that may affect the obliteration method used by the tactile plan—for example, the state of the arterial wall, regarding which investigations have been carried out by many workers in this country, by Russell, Oliver, Herringham, Hill and his collaborators, and by ourselves; in America by Janeway and Park, etc. In a former investigation we reached the conclusion that the condition of the arterial wall plays no important part in the vast majority of blood pressure estimations, either in the healthy state or in diseased conditions, but that in a certain number of cases with resistant brachial arteries, exaggerated readings of systolic pressure may be obtained. In these cases the method of continued local compression, as already described, is found to be very valuable in minimizing the chance of error. We close the brachial artery by digital pressure (two fingers) about the middle of the arm for from two to three minutes, and then at once reapply the armlet and take another systolic reading. Resistance of the arterial wall, if present, is thus almost completely set aside, and a corrected reading of systolic blood pressure is obtained. When the artery feels resistant to palpation (it may be noted in passing that the condition of the radial artery is no sure guide to the condition of the brachial, the latter being very frequently in a worse state) we first make an obliteration reading in the usual way, then slip down the armlet sufficiently to enable digital pressure to be applied as above stated; the armlet is then put in position again and the second reading taken. In this way it is commonly possible to equalize readings which at first gave widely differing values in different arteries, the high readings from a resistant artery being reduced to the level found in a non-resistant one, but not below that level; further compression induces no further reduction. This method does not equalize the arm-leg readings in cases of aortic regurgitation.

Estimation of Diastolic Pressure.

Comparatively little attention is given at present to diastolic pressure, a fact that is not surprising in view of the very general conviction that no practicable and reliable method of estimating it is available. Some years ago Professor C. J. Martin expressed an emphatic opinion that the systolic pressure is the only one that can be estimated with any accuracy—a conclusion affirmed also by many other observers, and widely accepted at the present time.

In the study of diastolic pressure the methods that have been most frequently used are those based on the principle of maximum oscillation or pulsation—Marey's principle, namely, that when the intra-arterial pressure is counterbalanced by an equal extra-arterial pressure the artery will pulsate most largely, showing maximum volume oscillations at the pulse-beats. The application of this principle has been studied by Mosso, Roy and Adami, Hill and Barnard, Recklinghausen, Howell and Brush, Erlanger, Martin, and others. For a statement of the conflicting views that have been held as to the relation of the oscillation to the internal pressure—whether diastolic or mean pressure, etc.—we must refer to our paper in *Heart*, 1914, v, 153.

In the same paper we comment on some other methods (Strassburger, Masing, Sahli, and others), worked on a different plan, and depending on the recognition (by finger or sphygmograph), not of volume changes in the length of artery compressed by the armlet, but on changes in the artery distally to the armlet.

The Diastolic Index by the Auditory Method.

A circulatory schema was arranged so that the actual systolic and diastolic pressures within an excised surviving artery were measured by maximum and minimum manometers, graphic records of pulsation or volume oscillation being obtained and the concomitant auditory phenomena being examined while the artery, enclosed in a tube or miniature "armlet," was subjected to various degrees of compression.

We have correlated the results obtained from this experimental schema under precise conditions with those yielded by an extended series of observations made in normal and pathological conditions in man by one of us (G. S. M.) in conjunction with Mr. J. R. Murray, M.B., in which three methods were employed concurrently: (1) the auditory, (2) the ordinary tactile, and (3) the graphic method by the use of the Erlanger apparatus. (An account of this investigation will be published elsewhere.) We have also used the Pachon sphygmo-oscillometer and found it to be by far the best of the forms of apparatus (yielding visual indications) which we have employed. By an ingenious arrangement the aneroid capsule has an equality of pressures maintained on its outer and inner surfaces, and the middle movement indicating the range of oscillation is a very sensitive one. Of course, the spring manometer which shows the armlet pressure needs, as all such instruments do, to be checked by a mercury manometer from time to time. We frequently use the sphygmo-oscillometer in conjunction with an ordinary armlet applied to the arm, in preference to the narrower armlet applied round the wrist by Pachon. Unfortunately in some cases, as with the Erlanger apparatus, it is difficult to recognize a definite point of sudden and marked declension in the oscillation magnitude. But in many cases, where such declension was marked, the Pachon diastolic index represented by the level of armlet pressure immediately after the declension corresponded with remarkable exactness with the weakening and dulling of the sound which constitutes the auditory index; the oscillations of the needle and alteration in the sound varied together very strikingly. By using the data derived from these various sources we have been enabled to arrive at very definite conclusions as to the validity and the true interpretation of the results yielded by the auditory method.

We have stated as our index of diastolic pressure the weakening and dulling of the sound which occurs at a certain level in the process of lowering of the armlet pressure, in opposition to the widely accepted view that the extinction of the sound is to be taken as the diastolic index.

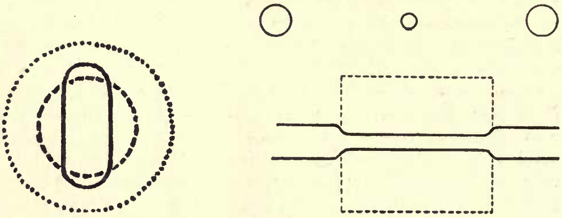
We find that the weakening and dulling coincides with the point at which the arterial tube just ceases to be flattened by the external pressure between the pulse beats. We ascertained, with the help of the experimental schema, that at this point the sound declines very markedly, the sharper sound evidently being produced by the sudden opening up by the systolic wave of the tube, which had been in some degree flattened by external pressure in the interval between the pulse beats; vibration associated with the sudden change in the shape of the tube is evidently responsible for the character of the sound. We have also had recourse to animal experiment for the verification of the auditory index.*

---

* An account of these results will be published elsewhere.

In Fig. 3 A the outer circle (dotted line) represents the size of the artery when distended by diastolic pressure—that is, in what we term the diastolic position. (The further expansion normally occurring with each systolic wave is relatively slight, and is not indicated here.) The inner circle (broken line) represents the undistended vessel, empty, or filled with blood at zero pressure—what we call the zero position, the position assumed by the arterial tube (between the pulse-beats) when the internal diastolic pressure is counterbalanced by an equivalent amount of external (or armlet) pressure.

With a further addition (an excess) of external pressure the vessel ceases to undergo diminution in the circular form, but becomes more or less markedly flattened. By the term "half flattening" we mean a condition where the distortion has reached such a point that the shorter diameter of the flattened tube is approximately one half of the diameter of the undistended circular vessel in the zero position. (See Fig. 3 A, unbroken line.) In a normally elastic artery such an increase of external pressure as induces half flattening between the beats elicits maximum oscillation of the arterial volume at each pulse-beat, accompanied by a very loud sound, often murmurish in character. In a relatively inelastic artery a greater increase of external pressure, inducing a degree of flattening greater than half flattening, is needed to elicit the maximum oscillation.


A Fig. 3. B

The persistence of the sound below the level of diastolic pressure—below the point where the external pressure is sufficient to cause some distortion of the tube from the circular form between the beats—is obviously due to sound production under conditions that differ in respect of the fact that the arterial tube retains its circular form all the time, there being no flattening between the beats. The length of artery embraced by the armlet is constricted (not flattened) by the external pressure. The influence of the external pressure is to counterbalance an equivalent amount of internal pressure, and produce an effect such as would result from a similar reduction of the internal pressure in the length of artery in question—that is, the length of artery embraced by the armlet would be less distended by internal diastolic pressure than the parts proximal to and distal to the armlet, as indicated in Fig. 3 B. At each systole there is a sudden expansion of the constricted tube, a much more extensive movement than the very slight systolic expansion of the unconstricted portions of the artery not embraced by the armlet. Possibly the chief seats of sound production are in the regions where the constricted and unconstricted portions become continuous.

In aortic regurgitation where the artery is suddenly expanded by the very large systolic wave sound commonly persists to very low levels and often to zero armlet pressure, being easily audible without the application of any external pressure at all.

Normal Diastolic Pressure and Pulse Pressure.

In the arms of a series of healthy young adults (examined in the sitting position) the average diastolic pressure was found to be about 65 mm. (with a range from 50 to 80 mm.) by the auditory method; this average differed little from that obtained from Erlanger tracings as interpreted by an index (not the same as Erlanger's) which we have adopted on experimental evidence. These values are much lower than those commonly stated for diastolic pressure.

In pathological subjects, on the other hand, there is much divergence between the auditory and the Erlanger results; we accept the former as more reliable, on evidence derived from various sources.

The average pulse pressure in the series of normal adults above referred to was about 46 mm.

Recognition of Differences in Diastolic Pressure induced by Gravity.

We have often been able to estimate in similar fashion the diastolic pressure in the lower extremity, the armlet being placed upon the leg and the auditory tambour over the posterior tibial artery. The same procedure is followed in first comparing the auditory and tactile systolic indices and then ascertaining the auditory diastolic indication in the usual way. The diastolic reading, like the systolic, naturally varies according as the person is in the recumbent or in the erect position, or in the resting state. In the former case, in healthy individuals, with arm and leg at the same level, the diastolic index, like the systolic, is got at corresponding levels; the change in the sound over the posterior tibial artery is, as a rule, perfectly definite. In the standing or sitting positions, on the other hand, the diastolic pressure reading necessarily exceeds to a large extent that obtained from the arm, as also does the systolic reading.* Thus, in the sitting position, such diastolic readings as these were obtained—arm 75 mm., leg 125 mm. The vertical difference between the level of the two armlets was found to be 69 cm.; the leg pressure was necessarily augmented by the weight of a column of blood 69 cm. long. As this corresponds to a pressure 52 mm. Hg, it accounts for the difference in the arm-leg readings as compared with the equality (75 mm.) found in arm and leg in the recumbent position. These results are confirmatory of the accuracy of the auditory method for both systolic and diastolic pressures with considerable differences in the conditions present, with blood pressures at very different levels, etc. Correspondence of *tactile systolic* readings in arm and leg, hydrostatic difference being allowed for, was found some time ago by Hill and Flack, and verified in our own observations.

---

* The systolic auditory reading was 115 in the arm and 165 in the leg; the pressure difference between the systolic and diastolic levels (pulse pressure) was thus equal (40 mm) in arm and leg.

Von Recklinghausen had postulated such correspondence. Similarly when the subject is lying down (in the horizontal position, or with the head lowered), and one leg is flexed at right angles to the trunk, the diastolic reading got from the lower part of the leg shows a reduction in accordance with the hydrostatic difference.

The influence of the altered conditions induced by local warming and cooling was also tested. Estimations were made before and after a limb had been kept immersed for some time in hot or cold water; the readings were compared with those made simultaneously on another limb. Sometimes one limb was warmed and another cooled, and a comparison made between the two. No appreciable difference was found in the readings under these different conditions.

We have also compared the auditory indications with those yielded by the oscillation method in (1) arm and leg at the same level, (2) arm and leg at different levels, and (3) leg at different levels, with results similar to those obtained in the arm.

The Auditory Method in Cases of Aortic Regurgitation.

The frequent presence in this disease of the well-known sounds (systolic thud or double murmur) audible without the application of any armlet pressure introduces new conditions. But the presence of such sound does not, as a rule, interfere with the recognition of the diastolic index, the sudden weakening and dulling being usually very well marked.

Comparison of Tactile and Auditory Systolic Indices as Means of Avoiding Certain Fallacies.

This comparison is essential is connexion with the estimation of both systolic and diastolic pressures. In regard to the former cases of difficulty occur, though rarely. An armlet pressure (for example, 300 mm.) very much above what is needed to obliterate the pulse, as tested by the tactile method (for example, 183 mm.), may fail to abolish the sound in the usual way, the sound being conducted past the obliterated area of artery, probably along the bone. Obviously the usual systolic index afforded by the upper limit of the sound is not applicable in such cases. While the armlet pressure is being lowered from a level far above the tactile systolic level a sudden increase in the intensity of the sound with the usual relation to the tactile index may occur and constitute, in all probability, the true systolic index in these instances. Such conditions have been noticed by one of us (G. S. M.), in conjunction with Mr. J. R. Murray, in a case of aortic regurgitation, and in one healthy student, a good athlete, in whom the sound at the elbow was found to persist at levels of armlet pressure far above what was necessary to obliterate the brachial artery as evidenced by the tactile method.

The estimation of diastolic pressure is not interfered with in such cases, the usual index being easily recognizable.

The comparison in question at once reveals inefficient working of the auditory method, due to an incorrect situation of the auditory tambour, stasis of blood in the limb from excessively and quite unnecessarily prolonged compression,* or the existence of an artery of insufficient size; both systolic and diastolic auditory indications may be vitiated by such conditions, though cases of unavoidable difficulty seem to be very rare. Danger of erroneous interpretation is readily obviated in the way stated. The applicability of the auditory method to the forearm has to be determined in this way; in some instances it fails, in others it gives quite satisfactory results.

The same test is essential in applying the method to the small arms of children; down to the age of 8 years we have obtained surprisingly good results in these.

Advantages of the Auditory Method.

The simplicity, ease, and rapidity of this method are strong points in its favour. It gives all the information that is to be obtained by more cumbrous and time-consuming methods, and that with greater precision, the index being a much sharper one than is present in other methods; it also causes less disturbance to the patient than slower methods, which involve a longer compression with the armlet. In the cases where the Erlanger or the Pachon apparatus give dubious or unreadable indications, the auditory method has always in our experience given a definite verdict. It is greatly superior to the palpatory and sphygmographic methods that have been proposed. We are satisfied that all the evidence as to diastolic pressure gained by the other methods, and much more also, can be better obtained by the quick and simple auditory method. The diastolic estimation in this way is as easy as that of systolic pressure, and is relatively little, if at all, complicated by certain sources of fallacy (for example, state of arterial wall) which may come into question in systolic estimation.

This method, measuring the diastolic as well as the systolic pressure, has the great advantage, as compared with the ordinary tactile method, of giving the numerical range of pressure variation in the artery during the whole cycle of the pulse beat, that is, the pulse pressure range.

---

* The accuracy of the auditory indications may be seriously impaired from this cause if the compression be unduly prolonged.

BIBLIOGRAPHY.

Erlanger and Hooker, *Johns Hopkins Hosp. Reports*, 1904, xii, 346. Gesell, *Amer. Journ. Physiol.*, 1913, xxxii, 70. Hooker, *Arch. of Intern. Medicine*, 1910, v, 491. Osler, *Principles and Practice of Medicine*, London, 1909, 797. Further references are to be found in *Heart*, 1913–14, iv, 317 and 408, and v, 153.

SYSTOLIC AND DIASTOLIC BLOOD PRESSURES IN AORTIC REGURGITATION.

BY

J. R. MURRAY, M.B.,

ASSISTANT IN PHYSIOLOGY IN THE UNIVERSITY OF ABERDEEN.

(From the Physiological Laboratory.)

THE arm-leg differences in the obliteration readings of systolic blood pressure observable in cases of aortic regurgitation when one armlet is applied to the upper arm and another to the calf of the leg are now very well known. Such discrepancy was first described by Hill, Flack and Holtzman,[3] and later by Hare,[2] Hill and Rowlands,[4] Rolleston,[9] and others, the tactile method being employed to detect the disappearance and reappearance of the pulse. In view of the remarkable differences observed, sometimes amounting to as much as 100, 150 mm. Hg, or more, the question naturally arises as to what is the "blood-pressure,"* and whether the arm or leg reading is the better indication of the aortic systolic pressure. The conditions are strikingly in contrast with those obtaining in the normal subject, the systolic arm-leg readings in the latter, tested in the same way (in the recumbent position with arm and leg at the same level), being equal. It may be recalled that in presumably normal animals under experimental conditions Hürthle, using his spring manometer, recorded higher systolic pressures in the femoral than in the carotid artery, and this was confirmed by Dawson working with valved manometers. But no evidence has been advanced to show the existence of such conditions in the normal human subject.

Nearly a year ago, when studying blood pressures in aortic cases, I observed some further differences of other kinds, and have repeated these observations many times, in 20 cases of aortic regurgitation. These differences affect both systolic and diastolic pressures in the different segments of the upper and lower limbs—quite a different matter from the arm-leg discrepancy in the tactile *systolic* readings from the upper arm and calf of the leg, above referred to.

METHODS.

In the present inquiry the systolic estimations were made by the auditory and tactile methods used in combination as already described by MacWilliam and Melvin[7]; the diastolic readings were obtained by the auditory method, using the sudden dulling and weakening of the sound as the diastolic index, after the application of the auditory method had been verified by comparing the auditory and tactile indices and finding the former to be at least as high as, or rather higher than, the latter. The oscillatory method, with the aid of the Erlanger and the Pachon apparatus, was sometimes employed for purposes of comparison.

---

* Rolleston noted a difference of 210 mm. in one case and 195 mm. in another.

For the arm, forearm, and leg, a 12 cm. armlet was used; for the thigh a broader one (17 cm.) except in cases where the thigh was a small one. The two armlets were compared and found to give identical readings on normal subjects.

When the armlet was on the upper arm the auditory tambour was placed near the bend of the elbow in the usual way, while the tactile reading was made from the radial artery; with the armlet on the forearm, both auditory and tactile indications were got from the radial artery. In the case of the thigh, the popliteal artery was used for the auditory, and the posterior tibial or dorsalis pedis for the tactile indices.* The popliteal artery was found to be too deep for satisfactory tactile examination; sometimes the auditory indications obtained from it were of doubtful reliability, and in such cases they were not taken as giving precise numerical values.

In some persons (normal and diseased) the forearm does not give satisfactory results by the auditory method; the applicability of the method has first to be tested in each case in the way stated—by comparison of the auditory and tactile indices. In aortic regurgitation the forearm commonly gives perfectly definite and satisfactory indications.

In examining the limbs two plans were employed. In one two armlets were used, one on the upper arm on one side, and the second on the forearm on the other side, the two armlets being connected with one inflator and manometer. Simultaneous estimations were thus made in the arm and forearm.

By the other plan one armlet was used successively upon arm and forearm, the observations being repeated and the two segments examined alternately to prevent danger of fallacy from a change in the pressure occurring during the observations. The results were relied upon only when the pressure in one segment was found to be unchanged on returning to it after examining the other. Often these alternate estimations were made several times, and, as a rule, with very constant results. In these circumstances there is no reason to doubt the accuracy of the values obtained by the method of successive (or alternate) examination; any other view would involve the preposterous assumption that changes were occurring in the actual diastolic pressure in such a way that the readings from the arm taken at intervals maintained one value, while those from the forearm taken alternately showed another constant value.

The terms "proximal" and "distal" segments of the limbs are applied to the upper arm and thigh, and to forearm and leg respectively, in the sense of these being proximal and distal portions of the limbs that are available for the application of an armlet to test the obliteration pressure in the usual way.

---

* The tactile index from the posterior tibial and dorsalis pedis (used in Table I) is, of course, a perfectly valid one, comparable to the use of the radial index with compression of the upper arm.

RESULTS.

The notable differences in systolic and in diastolic pressure found to exist in the upper and lower limbs, and in different segments of these limbs in aortic regurgitation, are in contrast with the results obtained by the same methods, applied in similar fashion, to normal persons. (The subjects were, of course, examined in the recumbent position.)

New facts were also brought out in connexion with the behaviour of the sounds heard in different arteries in cases of aortic regurgitation, (*a*) without the application of external pressure and (*b*) with varying amounts of armlet pressure.

The sharp differentiation of the inequalities of pressure about to be described affords further illustration of the precision of the auditory indications.

Differences in Systolic Pressure.

By the tactile method it is easy to determine not only the existence of higher pressures in the lower extremity than in the upper, but also, as a rule, higher pressures in the distal than in the proximal segments of the upper and lower limbs. This is shown in the subjoined tabular statement of a number of cases. It is to be noted in those instances in which there is little or no difference in the arm-forearm readings—as in Nos. 9, 10, 12—there is, as a rule, little or no difference in the thigh-leg values.

In No. 8, where the forearm tactile reading is lower than the upper arm, and where there is no appreciable thigh-leg difference, the diagnosis of aortic regurgitation was a very doubtful one. Moreover, in this case there was virtual agreement between the auditory systolic readings in the two limb segments—that is, forearm =120 mm. and upper arm=122 mm.

In Table II comparative pressures in the upper limb are stated. The forearm systolic average is 7.4 mm. above the upper arm by the tactile and 7.8 mm. by the auditory method.

Table III gives comparative values in the lower limb. The average systolic reading from the calf is 16 mm. above the thigh average by the tactile and 24 mm. by the auditory index.

From the above figures it is evident that the differences in systolic values between the proximal and distal segments of the limbs by both the methods, while not extensive, are perfectly definite and very appreciable. They stand in sharp contrast to what is found in normal limbs examined in the same fashion; in the latter the pressure differences, while not extensive, are distinctly in the opposite direction—that is, the average readings from the proximal segments are appreciably higher than those from the distal segments.

The higher systolic pressures in the distal segments of the limbs may be interpreted as being due to an augmentation of the height of the systolic wave by a reflected wave from the periphery. Such augmentation can be easily demonstrated, as occurring under certain conditions, with a circulatory schema. Von Kries[6] and Tigerstedt[10] suggested an explanation of this sort to account for the

TABLE I.—*Tactile Systolic Readings in Aortic Regurgitation.*

No.	Pulse-rate.	Fore-arm.	Upper Arm.	Calf.	Thigh.
1	85	112	109	148	—
2	65	193	182	280	262
3	87	134	116	158	140
4	75	138	134	173	154
6	112	150	130	190	—
7	86	170	163	230	189
8	74	106	122	126	120
9	64	125	124	206	202
10	72	132	133	183	182
11	84	124	120	—	164
12	67	184	182	200	198
13	70	170	172	185	175
17	80	135	125	194	174
18	94	156	136	182	150
19	76	200	182	296	226
Average ...	79.4	148.6	142	196.5	179.7

TABLE II.—*Comparative Pressures in the Upper Limb.*

No.	Forearm.			Upper Arm.		
	T.S.	A.S.	A.D.	T.S.	A.S.	A.D.
1	128	130	62	130	130	55
2	193	214	65	182	200	65
3	134	134	78	120	126	60
8	106	120	78	118	122	74
9	125	135	62	124	135	45
12	184	204	80	182	210	75
14	142	156	75	135	145	65
15	194	198	105	194	196	95
16*a*	180	182	102	154	180	92
16*b*	136	140	85	135	135	78
17	137	150	50	125	127	40
18	156	170	80	136	142	50
19	200	210	75	182	194	70
Average ...	155	164.8	76.6	147.6	157	66.4

TABLE III.—*Comparative Pressures in the Lower Limb.*

No.	Calf.			Thigh.		
	T.S.	A.S.	A.D.	T.S.	A.S.	A.D.
2	280	300	72	262	240+	72
4	173	184	66	154	172	54
8	126	130	96	120	126	82
12	200	210	100	198	220	98
17	194	220	50	174	190	44
18	182	212	70	150	164	50
Average ...	192.5	209.3	75.6	176.3	185.3	66.6

higher systolic pressures that have been observed under experimental conditions in animals in the femoral artery as compared with the carotid (Hürthle,[5] Dawson[1]). The systolic differences between the limb segments above referred to are, of course, very small in amount compared to the difference between the upper and lower limbs that has been found in cases of aortic regurgitation.

Comparative values of systolic pressures in the proximal and distal segments of the upper and lower limbs obtained by the tactile and auditory methods are contained in Tables II and III, Nos. 2, 8, 12, 17, 18, the averages of which are given later. (The auditory diastolic results included in the tables are dealt with later.) In these it is seen that the systolic averages by both methods come in a descending series—(1) calf, (2) thigh, (3) forearm, (4) upper arm, the calf reading being about 50 mm. by the tactile and 54 mm. by the auditory method above the average for the upper arm, while the thigh and forearm show intermediate values. The thigh exceeds the upper arm by 32 mm. by the tactile and 26 mm. by the auditory index; the forearm exceeds the arm by 7 mm. by the tactile and 11 mm. by the auditory method.

Differences in Diastolic Pressure.

It is agreed by all observers that the diastolic pressure readings obtained from the various accessible arteries are practically equal in the normal state. It has been found by careful measurements with valved manometers, as in Dawson's[1] investigation, that the diastolic pressure is practically constant throughout the larger vessels, with the exception that the femoral pressure has been found to be slightly lower (by 8 mm.) than the carotid. Thus the innominate and the brachial arteries showed identical readings (for example, 101 mm. Hg, in the dog.)

Even in abnormal conditions there is little evidence of discrepancy. Oliver,[8] using the oscillatory method with an armlet, recorded certain differences between forearm and arm in some aged (nonagenarian) persons; these differences were very slight in amount (5 mm. or less), and were in favour of the upper arm.

In the present investigation very notable differences in diastolic readings were obtained from different arteries by the auditory method; the oscillatory method (especially the Pachon sphygmo-oscillometer) was also often employed. When the Pachon apparatus gave quite unequivocal indications (which was not always the case) these corresponded closely with the auditory results.

A series of levels of diastolic pressure was found to exist, the pressure being lower nearer the heart and rising in value in the more distally-situated arteries, and ascending series of values being obtained in the following order, (*a*) upper arm, (*b*) forearm and thigh, and (*c*) calf of leg.

This is shown by comparing the different values obtained in the four segments in 5 cases in which the readings from all the four segments were considered entirely satisfactory in the same individual. The averages for these 5 cases are as follows:

	Forearm.	Upper Arm.	Calf.	Thigh.
Systolic	155.2	148.6	198.4	180.8
Diastolic ...	70.6	60.8	77.6	69.2

This relationship of the various diastolic levels is clearly indicative of the influence of the valvular leak at the beginning of the arterial tube telling more markedly in lowering the diastolic pressure the nearer the artery is to the heart.

The tabular statements already given (see Tables II and III) show decidedly lower diastolic pressures in the proximal than in the distal segments. The average difference in Table II between arm and forearm is seen to be 10.2 mm., and in Table III between thigh and leg 9 mm. (The averages in Tables II and III cannot be compared as they do not both include the same cases, Table II containing many more than Table III.)

It is obviously important to make a careful comparison with the same apparatus and under similar conditions between the limbs of normal subjects and those of persons suffering from aortic regurgitation and other morbid conditions.

Examples of Simultaneous Estimation of one Upper Arm and the other Forearm.

	Forearm.	Upper Arm.
(*a*) Aortic regurgitation.		
(1) Auditory systolic	140	135
,, diastolic	85	78
(2) Auditory systolic	140	138
,, diastolic	85	75
(3) Auditory systolic	140	133
,, diastolic	85	75
(*b*) Normal.		
Auditory systolic	119	120
,, diastolic	80	80
(*c*) Pathological (nephritis) with no aortic regurgitation.		
Auditory systolic	170	162
,, diastolic	110	110

Similar diastolic values were obtained in these three cases by the Pachon sphygmo-oscillometer.

Behaviour of the Sound heard in the Arteries.

Occurrence of Sound without External Pressure.—In some cases the systolic sound is heard in all the arteries (brachial, radial, popliteal, posterior tibial, and dorsalis pedis) without the application of armlet pressure at all. In other instances the sound is audible in some, but not all, of these; it is absent (*a*) most frequently in the posterior tibial and dorsalis pedis, (*b*) next in the radial, (*c*) least frequently in the brachial. The presence of sound in the arteries, apart from the application of external pressure, is strongly suggestive of aortic regurgitation; but, on the other hand, the sound is often absent in this disease—at least, in the limb arteries, the brachial being the seat of its most common occurrence as far as the limbs are concerned. The fading away of the sound is apparently related to distance from the heart. The fact that this systolic sound is frequently present in the carotids while absent in any of the limb vessels affords further proof of this. With regard to the double murmur of Duroziez, I have found it present in all the limb segments in one patient—a patient who was in the last stages of aortic disease and who died about six hours after the observations were made. In this patient the double character of the murmur was extinguished when the external pressure was raised slightly above the systolic pressure as indicated by the tactile method, a single sound persisting.

Persistence of Sound Below the Diastolic Index under the Influence of External Pressure.—In the series of auditory phenomena this constitutes what is commonly termed the fourth phase—that is, the phase between (*a*) the change from a clear to a duller weakened sound, and (*b*) the extinction of the sound (fifth phase). As the armlet pressure is being lowered and the diastolic index has been passed (beginning of the fourth phase), the sound, even when the armlet pressure has fallen to zero, may persist in some arteries, while it may disappear much earlier in others—that is, at higher levels of armlet pressure. Such levels vary in different limbs and segments of limbs. With the armlet in different situations the extent to which the sound persists below the diastolic index is (*a*) greatest in the upper arm, (*b*) next in the forearm, and (*c*) least in the calf of the leg. The rule seems to be that the sound disappears earlier in the distal segment of a limb than in the proximal one, and in the lower limb earlier than in the upper. (It has been already stated that the precise values obtained from the popliteal arteries are in some cases open to question, but the broad relation between the results got with the armlet on the thigh and the leg respectively are clear enough.) Thus there may be abolition of the sound at armlet pressures of 30 mm., etc., in the leg, while in the arm and forearm the sound continues to be audible even after the armlet pressure has been reduced to zero. The sound often persisted down to zero in the upper arm, though extinguished in other parts while the armlet pressure was still at considerable heights—for example, in one case 80 mm. on the leg and 60 mm. on the forearm; in another case, 53 mm. on the leg and 38 mm. on the forearm; in a third, 70 mm. on the leg and 60 mm. on the forearm.

Duration of Persistence of Sound below Diastolic Index in Limb Segments.

The extraordinary variability in the levels of armlet pressure at which the sound disappears in different limb segments constitutes additional evidence that the lower limit of the sound cannot be taken as an index of diastolic pressure; according to such an index the diastolic pressure would be represented as varying in the different arteries in an obviously impossible fashion.

In the leg extinction of the sound may almost immediately follow the change which constitutes the diastolic index, while in the arm of the same person the sound may persist till the armlet pressure has fallen to a much lower level.

Differences (in mm. Hg) between Diastolic Index and Extinction of Sound.

Number.	Forearm.	Upper Arm.	Calf.
1	3	7	—
2	15	5	7
3	—	10	10
4	—	4	6
8	—	18	9
9	62	45	34
10	8	45	5
12	10	15	10
13	—	20	20
15	15	7	—
16	32	67	—
17	10	30	20
18	20	50	—
19	15	70	10
Average ...	13 5	28.0	9.3

In order to test the influence of a regurgitant leak at the central pump upon the pressures at different distances along the stream, experiments were performed with a circulatory schema, similar in a general way to that described in former papers from this laboratory.[7]

A syringe, worked in regular fashion by a motor, supplied a pulsating stream through the schema. At two points in the stream at different distances from the pump sets of valved manometers, proximal and distal, were connected so as to measure the pressures, especially the minimum of diastolic pressure at these points. The relation of the pressures in the proximal and distal manometers was determined when the pumping syringe was provided with efficient valves. Comparative observations were then made after valvular defect, causing regurgitation into the syringe, had been induced. It was found that the diastolic pressure in the proximal manometer was reduced relatively to that in the distal manometer, the fall of pressure, induced by regurgitation, at the central end or origin of the pulsating stream telling on the proximal portion of the stream and its associated manometer more than on the more distal portion and its manometer.

I have to record my thanks to Professor MacWilliam for much kind assistance and advice during this investigation, and also to the honorary staff of the Aberdeen Royal Infirmary (where the clinical part of this investigation has been carried out) for permission to investigate the cases in their wards.

REFERENCES.

[1] Dawson, *Amer. Journ. Physiol.*, 1905–6, xv, 244. [2] Hare, *Therap. Gazette*, 1910, third series, xxvi, 457. [3] Hill, Flack and Holtzman, *Heart*, 1908–9, i, 73. [4] Hill and Rowlands, *Heart*, 1911–12, iii, 219. [5] Hürthle, *Arch. f. d. ges. Physiol.*, xlvii, 32. [6] Von Kries, *Studien zur Pulslehre*, Freiburg, 1892, 67–68. [7] MacWilliam and Melvin, *Heart*, 1914, v, 153. [8] Oliver, *Studies in Blood Pressure*. London, 1908, 119–120. [9] Rolleston, *Heart*, 1912, iv, 83. [10] Tigerstedt, *Lehrb. der Physiologie des Kreislaufes*, Leipzig, 1893, 352.

ON THE RESISTANCE OF TRYPSIN SOLUTIONS TO HEAT.

By EDWARD STAFFORD EDIE.

From the Physiological Department.

The action of heat on aqueous solutions of many enzymes has been studied more or less carefully for many years, and the general conclusion arrived at has been that all enzymes in aqueous solution are destroyed when heated for a short time to about 70° or 75°. So much is this the case that frequently the activity of a substance after its solution has been heated has been taken as proving that the substance in question is not an enzyme (e.g. secretin).

Since trypsin is practically without any digestive action in acid or neutral solution, the effect of heat on this enzyme was at first tested principally in alkaline solution, and it was found that such a solution rapidly became inactive at as low a temperature as 50° or sometimes even at 45° [Biernacki, 1891]. Vernon [1901] also found that fresh preparations of trypsin lost more than half their activity when kept in 0·4 % sodium carbonate at 37° for an hour. Similar results have been found by Vernon in later experiments, and by other observers.

On the other hand Vernon [1904] found that the presence of protein protected trypsin solutions from the effect of heat to a considerable extent, and the same protection was afforded by proteoses or peptone. Bayliss and Starling [1903] had previously noticed the protective effect of proteins or their hydrolytic products on solutions of trypsin.

The action of acids on trypsin, however, has not been so fully studied. Langley [1881] found that trypsin was considerably weakened by warming its solution for 2½ hours with 0·05 % hydrochloric acid. Wróblewski, Bednarski and Wojczynski [1901] found that trypsin when kept at 37° for a few hours in hydrochloric acid of over 0·14 % was considerably affected, and if 0·56 % acid were used the enzyme was sometimes completely destroyed.

The question of the effect of heat on trypsin was investigated later by

Schmidt [1910], who stated that trypsin in a slightly alkaline solution containing 5 % of peptone could be boiled without being destroyed. The same protection against heat was afforded by a 2 % solution of agar or a 10 % solution of gelatin. Schmidt also stated that if trypsin powder were suspended in water-free glycerol it could be heated to 292° without being destroyed or much affected.

Schmidt's work was repeated by de Souza [1911], who however found that 5 % peptone had hardly any effect in protecting trypsin solutions from destruction by heat. It appears from these experiments that an appreciable protection is afforded by 20 % peptone under certain conditions, but if the heating is sufficient to cause complete destruction of the trypsin in pure aqueous solution, then the presence of peptone has only a slight protective effect. De Souza also tried the effect of heat on trypsin in presence of 20 % peptone in acid, neutral and alkaline solutions. The solutions were heated to 80° for five minutes. No difference was observed between the acid and neutral solutions, the activity of these after heating being however slightly greater than that of the alkaline solution. Even in the case of the acid or neutral solution, however, over 85 % of the trypsin was destroyed, and about 90 % in the case of the alkaline solution.

Ohta [1912] also repeated the experiments of Schmidt, but failed to confirm his results.

In a paper just published, Mellanby and Woolley [1913] find that while trypsin is readily destroyed by heat in neutral or alkaline solution, if a solution of trypsin be made slightly acid, say with hydrochloric acid, it can be boiled for five minutes and yet retain considerable digestive power.

According to these observers, trypsin is destroyed in acid, more rapidly than in alkaline or neutral solution up to about 40°, but at higher temperatures the reverse is the case. At 40° there appears to be an optimum protective concentration of acid, above or below which the rate of trypsin destruction is accelerated.

Before the publication of the work of Mellanby and Woolley, and unaware of their experiments, I had tested the effect of heat on trypsin in connection with another research, and obtained results of a similar character. The method of testing the digestive power of the trypsin solutions was that of Hedin [1903]. The trypsin was allowed to act on a solution of caseinogen in presence of toluene and after a definite interval excess of tannic acid was added, to precipitate unaltered protein, meta-protein and proteoses. After standing 12 hours or more the precipitate was filtered off and the nitrogen determined in a portion of the filtrate by Kjeldahl's method. Controls were also carried out to show the effect, if any, of the alkali used on caseinogen, and the amount of nitrogen not precipitated by tannic acid was also determined in each solution of trypsin used.

The following are the principal results obtained:—

1. Benger's Liquor Pancreaticus used as trypsin solution, 10 cc. of this requiring 1·6 cc. of N/10 sodium hydrate for neutralisation. 2 °/₀ caseinogen in normal sodium carbonate was the substrate. A portion of the trypsin was boiled for three minutes and cooled before adding the caseinogen. Digestion was continued at 37° for three hours.

		Digestion in cc. of N/10 nitrogen not ppted by tannic acid
(*a*)	1 cc. trypsin, 20 cc. water, 40 cc. caseinogen	49·8
(*b*)	1 ,, (boiled) ,, ,,	29·7

In this experiment the effect of boiling trypsin in slightly acid solution was to leave 60 °/₀ of the original digestive power unimpaired.

2. 10 cc. of the above trypsin solution were neutralised with sodium carbonate and made up to 25 cc. with water. Three portions (*a*, *b* and *c*) were boiled for three minutes in neutral, alkaline and acid solution respectively, cooled, and kept at 37° with 20 cc. of 2 °/₀ caseinogen in 2 N sodium carbonate for three hours.

		Digestion in cc. of N/10 nitrogen not ppted by tannic acid
(*a*)	2·5 cc. trypsin, 20 cc. water...	0·2
(*b*)	2·5 cc. trypsin, 19 cc. water, 1 cc. N Na_2CO_3 ...	0·1
(*c*)	2·5 cc. trypsin, 19 cc. water, 1 cc. N HCl ...	20·8
(*d*)	2·5 unboiled trypsin, 20 cc. water	20·9

It may here be mentioned that in all the experiments carried out, any differences in reaction due to the trypsin being boiled in acid etc. were adjusted before the caseinogen was added. Special care was taken also to ensure that none of the trypsin escaped being heated to 100°.

In the above experiment it will be seen that after being boiled in acid solution for three minutes, the trypsin still retained all its power of digesting caseinogen, while boiling in alkaline or neutral solution had completely destroyed the enzyme.

The digestive power of this trypsin before and after being boiled as above was also tested on boiled ox fibrin, the amount of nitrogen in the filtrate from the undissolved fibrin at the end of the digestion being taken as the measure of the action of the enzyme. It was found that on such fibrin trypsin acts only slowly, producing much less effect in a given time than when acting on caseinogen. Nevertheless the trypsin boiled in acid dissolved as much fibrin as the unboiled trypsin, while that boiled in neutral or alkaline solution again had no digestive power.

3. Merck's trypsin used. A weak solution of this trypsin was dialysed against running water for 18 hours and filtered. The solution was neutral. The trypsin contained 0·02 °/₀ nitrogen. Three portions were boiled for three minutes (*a*, *b* and *c*) and then allowed to act on 20 cc. of 2 °/₀ caseinogen in 0·4 N Na_2CO_3 at 37° for three hours.

		Digestion in cc. of N/10 nitrogen not ppted by tannic acid
(*a*)	25 cc. trypsin, 1 cc. N Na_2CO_3	0
(*b*)	25 cc. trypsin, 1 cc. water	0·2
(*c*)	25 cc. trypsin, 1 cc. N HCl	21·4
(*d*)	25 cc. unboiled trypsin	28·9

In this experiment 75 °/₀ of the original digestive power remains after boiling the trypsin in acid solution, but the trypsin is destroyed in neutral or alkaline solution.

For the rest of the experiments the trypsin used was prepared in the method described by Hedin [1905]. An ox pancreas was minced and allowed to undergo autolysis at 37° in presence of water and toluene for a day and filtered. The filtrate was again kept at 37° for two days, dialysed against running water for two days, filtered, and kept with a little toluene.

This trypsin solution was neutral, contained less than 0·01 °/₀ nitrogen, and gave practically no biuret reaction.

4. Three portions of this trypsin were boiled for three minutes, and cooled before adding 20 cc. of caseinogen (same as in last experiment). Digestion lasted three hours.

		Digestion in cc. of N/10 nitrogen
(*a*)	25 cc. trypsin, 0·5 cc. N/10 Na_2CO_3	0·2
(*b*)	25 cc. trypsin, 0·5 cc. water	0·2
(*c*)	25 cc. trypsin, 0·5 cc. N HCl	6·5
(*d*)	25 cc. unboiled trypsin	10·5
(*e*)	Control (water + caseinogen)	0

In this experiment we see that over 60 °/₀ of the original digestive power of the trypsin survives after the acid solution has been boiled, but none in the case of the neutral or alkaline solutions, the 0·2 cc. being within the limits of experimental error.

5. In order to see to what extent this trypsin would survive more prolonged heating, 25 cc. of the solution together with 5 cc. of N/10 HCl

were brought to boiling in a flask and then put in a steriliser for 20 minutes. During the whole of this time the temperature throughout the interior of the steriliser was 100°. The contents of the flask were then cooled and neutralised.

To a fresh portion of 25 cc. trypsin 5 cc. of N/10 HCl were added, and immediately neutralised. Then to both flasks were added 20 cc. of the usual caseinogen solution.

25 cc. of water were treated in exactly the same way as the fresh portion of trypsin, and the flasks were kept at 37° for 4·25 hours.

		Digestion in cc. of N/10 nitrogen
(*a*)	Boiled trypsin	4·2
(*b*)	Fresh trypsin	16·7
(*c*)	Control	0

The amount of nitrogen not precipitated by tannic acid, which was contained in the 25 cc. trypsin used, was also estimated, and allowed for in the above results. It corresponded only to 1 cc. of N/10 nitrogen.

From this experiment it appears that under suitable conditions a solution of trypsin can be heated to 100° for 20 minutes and yet retain 25 °/₀ of its original digestive power.

6. I have repeated one of the experiments described by Mellanby and Woolley to test the effect of varying concentrations of acid on trypsin. My experiment was carried out at 45°, at which temperature the acid solutions were kept for 15 minutes. 20 cc. of the usual caseinogen solution were added and digestion continued at 37° for three hours.

		Digestion in cc. of N/10 nitrogen
(*a*)	25 cc. trypsin, 0·2 cc. N HCl	8·0
(*b*)	25 cc. ,, 0·4 ,, ...	8·9
(*c*)	25 cc. ,, 0·6 ,, ...	8·9
(*d*)	25 cc. ,, 0·8 ,, ...	9·3
(*e*)	25 cc. ,, 1·0 ,, ...	8·9
(*f*)	25 cc. unboiled trypsin	9·8

In the above series the trypsin seems to be the least protected by the weakest acid (0·008 N), each of the other concentrations of acid having much the same effect. In all cases at least 80 °/₀ of the original digestive power remains after heating.

SUMMARY.

Solutions of trypsin when neutral or alkaline are rendered completely inactive by boiling.

Acid solutions of trypsin, on the other hand, after being boiled retain a considerable power to digest caseinogen. In some cases there is no destruction of this digestive power at all.

The power to digest caseinogen appears to be less affected by heat than the power to coagulate calcified milk, this being taken as the measure of the activity of trypsin by Mellanby and Woolley.

It may be that these two evidences of the action of trypsin are due to different sets of groupings of the trypsin molecule, and that the groupings to which the digestion of caseinogen are due are more thermostable than the others.

REFERENCES.

Bayliss and Starling (1903), *J. Physiol.* **30**, 61.
Biernacki (1891), *Zeitsch. Biol.* **28**, 62.
Hedin (1903), *J. Physiol.* **30**, 155.
—— (1905), *J. Physiol.* **32**, 468.
Langley (1881), *J. Physiol.* **3**, 246.
Mellanby and Woolley (1913), *J. Physiol.* **47**, 339.
Ohta (1912), *Biochem. Zeitsch.* **44**, 472.
Schmidt (1910), *Zeitsch. physiol. Chem.* **67**, 314.
de Souza (1911), *J. Physiol.* **43**, 374.
Vernon (1901), *J. Physiol.* **27**, 269.
—— (1904), *J. Physiol.* **31**, 346.
Wróblewski, Bednarski and Wojczynski (1901), *Beiträge*, **1**, 289.

Blood-pressure estimation by the auditory method. By J. A. MacWilliam, G. Spencer Melvin, and J. R. Murray.

At a comparatively early stage in our investigation of methods of blood-pressure estimation in man, we had recourse to animal experiment, though we have not hitherto published any statement of such experiments having reference to the verification of diastolic pressure estimation by the auditory method.

In the case of small animals, the testing of the auditory method is not satisfactory, but in animals of sufficient size the procedure offers no special difficulty apart from those connected with respiratory disturbance associated with the anæsthetic. We have found the sheep a very suitable subject. The results are very definite and convincing.

The animal is anæsthetised with ether and chloroform, after a preliminary injection of morphia and chloral. A large-sized reservoir cannula is placed in the central end of the left carotid artery at the root of the neck, and is connected, by non-distensible tubing, with a set of manometers—valved ones for maximum and minimum pressures and a "compensated" one for mean pressure—so that the intra-arterial pressure can be brought to bear on any of the manometers as desired.

An ordinary armlet 12 cm. broad is applied round the neck, it being noted that the circumference of the latter is not too great for such a breadth of armlet. The armlet pressure being raised and lowered in the usual way, the auditory phenomena are examined by means of an Oliver tambour (phonendoscope) applied over the right carotid artery on the distal side of the armlet, the artery being left covered by the tissues with the exception of the skin.

In order to prevent disturbance from venous congestion of the head due to obstruction caused by the armlet pressure, the internal jugular vein is protected by a split lead tube (15 cm. long) which prevents its being compressed by the armlet pressure. A tracheal cannula was sometimes used.

One observer made the auditory observations and read off the armlet pressures from a mercury manometer, while another determined the intra-arterial pressures as shown by the valved manometers. The observers frequently changed places and repeated the estimations. The operative part of the experiments was performed by two of us (J. A. MacW. and G. S. M.).

The auditory phenomena were very marked and characteristic, the phases corresponding with those found in man and in a circulatory schema. The systolic auditory index was found to be correct. The auditory diastolic index constituted by a sudden dulling and weakening of the sound at a certain point in the lowering of the armlet pressure proved a very accurate guide to the intra-arterial diastolic pressure as shown by the minimum manometer[1]. Extinction of sound was much later.

Considerable variations in pressure and pulse rate were induced in the course of the observations with no impairment of the accuracy of the results. The pressure was raised by mechanical compression of the abdomen, lowered by an increased dose of chloroform etc. Pulse rates varying from about 60 to 110 were present at the different phases.

We also tried the oscillatory method by connecting the armlet with the Erlanger sphygmomanometer and with the Pachon sphygmo-oscillometer, but found the indications more difficult to read than the auditory ones.

At the beginning of the observations before the armlet was inflated the pressures, as shown by the manometers, were Systolic 110, Mean 80, Diastolic 52, the mean pressure being only slightly different from the arithmetical mean.

Some experimental data are subjoined:

Observation	Intra-art. press. by valved manometers		Auditory diastolic reading	Remarks
	Systolic	Diastolic		
1	96	45	45	Much chloroform given.
2	96	51	50	——
3	98	54	50	——
4	96	56	53	——
5	96	60	60	——
6	102	84	80	Compression of abdomen. Pulse rate 110.
7	96	60	60	——
8	112	70	70	Compression of abdomen.
9	112	70	70	——
10	85	41	40	Dose of chloroform increased.
11	85	48	47	——
12	94	46	45	——
13	94	74	74	——
14	94	65	68	——
15	80	56	54	——

---

[1] We arrived at this conclusion on other grounds also, from experiments with a circulatory schema as described in *Heart*, 1914, v. 193, and from observations made on man in different circumstances—see a paper in the *Quart. Journ. of Exp. Physiol.* 1914, VIII. and one in the *Brit. Med. Journ.* March, 1914.

ACTION OF PEPSIN AND TRYPSIN ON ONE ANOTHER.

(Preliminary Paper.)

BY EDWARD STAFFORD EDIE.

From the Physiological Department.

Hitherto only a small amount of work has been done in investigating the action of enzymes on one another, and many of the earlier results are inconclusive or contradictory. It was stated by Corvisart (quoted by Wróblewski) that pepsin and trypsin were mutually destructive. Kühne [1876], on the other hand, found that pepsin digested trypsin, but that the reverse did not hold good. A few years later Engesser [1880] however found that pepsin had practically no action on trypsin, digestion being continued for two hours. Further uncertainty was introduced by the work of later authors.

Langley [1881] tested the action of certain enzymes on one another, taking the precaution to determine the action of acid or alkali of the appropriate strength on the enzymes in question. He found that pepsin was destroyed considerably more rapidly by trypsin in an alkaline solution than by alkali of the same strength acting on the pepsin alone. Langley also found that trypsin lost much of its digestive power when kept for some time in 0·05 % hydrochloric acid before being allowed to act on fibrin in alkaline solution, but he does not appear to have done any experiments himself to show the action of pepsin on trypsin. As the result of a considerable number of experiments on different enzymes, Wróblewski, Bednarski and Wojczynski [1901] conclude that not only does trypsin increase the destructive effect of alkali on pepsin, but also that pepsin increases the destructive effect of acid on trypsin. While different observers have found considerable variations in the range of hydrogen or hydroxyl ion concentration compatible with digestive power on the part of pepsin or trypsin respectively, there seems little doubt that the former enzyme has no appreciable action in an alkaline medium, trypsin on the other hand being active only in presence of alkali. Consequently previous investigations of the action of these enzymes on one another appear to have been confined to discovering if pepsin would digest trypsin in acid solution, or if trypsin on the other hand would have a destructive action on pepsin in an alkaline medium.

In the light of the older view that enzymes were of a protein nature it was not unreasonable to expect that in such cases the pepsin for example would in an acid medium break up the trypsin into a number of less complex substances, and that thus the specific digestive properties of the trypsin would be lost.

Now that considerable doubt has been thrown on the protein nature of the enzyme molecule, however, such a breakdown of the molecule is by no means certain to take place in every case.

Within the last few years the mode of action of enzymes has been rendered clearer by experiments which appear to show that the enzyme acts on its appropriate substrate by means of different chemical groups or side chains.

Pollak [1905] found that on diluting a trypsin solution with a quantity of the same trypsin solution which had been previously heated to 70° much less digestion took place than in the case where the enzyme was diluted with a corresponding amount of water. Similar results were obtained by Schwartz [1905] in the case of pepsin.

Bayliss [1904] found that trypsin became altered in the above way on being heated, and suggested that the altered enzyme or "zymoid" still retained the power of combining with the substrate, but that the specific digestive power had been destroyed.

Bearn and Cramer [1907] also found that pepsin and rennin when heated to about 60° inhibited the action of the fresh enzyme when excess of the heated enzyme was added. Generally it was found that if the enzyme were heated to 100° this inhibitory power was lost, the reason probably being that the groups which combine with the substrate are themselves destroyed at 100°. Different enzyme preparations, however, varied considerably in their resistance to heat.

Although trypsin is a more energetic proteolytic enzyme than pepsin, nevertheless they are both capable of acting on a large number of proteins with the formation of similar hydrolytic products to a certain stage of digestion. This led to the idea that both enzymes might attack proteins by combining with the same side chains, the specific digestive action of the enzymes, however, being due to dissimilar side chains, the latter in the case of pepsin acting only in acid solution, and in the case of trypsin only in presence of alkali.

If this were the case we should expect that an excess of trypsin would inhibit the action of pepsin in acid solution, and similarly excess of pepsin would inhibit the action of trypsin in alkaline solution. The enzyme present in excess in such cases would thus act in a manner analogous to the zymoid of the other enzyme.

EXPERIMENTAL METHODS.

Various enzyme preparations were used in these experiments, such as Benger's Liquor Pepticus and Liquor Pancreaticus, and the pepsin and trypsin in scales or powder of Merck, Fairchild and Grübler.

The enzyme solutions were put in small flasks and a definite amount of dilute hydrochloric acid or sodium carbonate added. In each flask was then put an equal amount of the protein to be digested and the flasks were kept in a water bath at 37° for a certain time. Any slight accidental variations in temperature would affect all the flasks equally, and thus introduce no difficulty.

Two methods of estimating the amount of digestion were employed. The first, principally used for determining the amount of digestion by pepsin, was that of making the mixture of enzymes act on fibrin for a definite time. The undissolved fibrin was then filtered off and the nitrogen in a portion of the filtrate determined by Kjeldahl's method.

Since the object of these experiments was to determine the activity of one enzyme under different conditions, for example the relative digestive power of pepsin in dilute acid and of pepsin in the same strength of acid containing trypsin in addition, such a method of estimating the amount of digestion seems quite satisfactory, as the stages of digestion must presumably be the same in both cases, and where digestion has gone on for a definite time the amount of dissolved nitrogen must give a true indication of the digestive power of the enzyme under these conditions. The fibrin was always obtained from ox blood, and was minced, thoroughly washed till free from blood, suspended in water and heated to 70° in order to destroy any enzymes present. The water was then pressed out and the fibrin preserved in glycerol. When the fibrin was required for use, the glycerol was washed out with water, the excess of water pressed out and equal weighed amounts of the fibrin taken for experiment.

Control experiments were also carried out with the same amount of fibrin and acid or alkali, but no enzyme. No appreciable amount of fibrin was found to be dissolved in any of the controls.

The amount of nitrogen present in the solutions of enzymes used was also determined in every case, and that amount deducted from the total nitrogen in solution at the end of the experiment. The difference represented the nitrogen of the protein dissolved by the enzyme.

The other method of determining digestive power employed in these experiments was that described by Hedin [1903]. The enzyme is allowed to act on a solution of caseinogen, and at the end of the period of digestion excess of tannic acid is added. The unchanged protein and proteoses are precipitated, and the nitrogen left in solution is estimated in the filtrate by Kjeldahl's method. This gives a measure of the amount of protein digested to the stage of peptone or amino-acids.

Control solutions of the enzymes and also of the caseinogen used were also treated in the same way with tannic acid, and the nitrogen in the filtrate allowed for in calculating the amount of protein digested. Toluene was added to each flask in order to prevent the action of bacteria. As a rule it was found that the fibrin method was the more suitable when digestion by pepsin was being studied, as pepsin digests caseinogen only very slowly to the stage at which it is not precipitated by tannic acid.

On the other hand, the caseinogen method was found more suitable for digestion by trypsin, the latter enzyme dissolving heated ox fibrin too slowly for convenience in experiment.

EFFECT OF EXCESS OF TRYPSIN ON THE DIGESTIVE POWER OF PEPSIN.

		Digestion in cc. of N/10 nitrogen
1.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	11·4
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	26·9
	1·4 g. fibrin added. Digestion 2·5 hours.	
2.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	9·0
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	26·3
	1·5 g. fibrin. Digestion 1·5 hours.	
3.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	9·9
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	28·8
	1·6 g. fibrin. Digestion 2·25 hours.	
4.	1 cc. pepsin, 10 cc. trypsin, 20 cc. water, 30 cc. N/10 HCl	37·1
	1 cc. pepsin, 20 cc. trypsin, 10 cc. water, 30 cc. N/10 HCl	14·2
	1 cc. pepsin, 30 cc. trypsin, 30 cc. N/10 HCl	5·8
	1 cc. pepsin, 30 cc. water, 30 cc. N/10 HCl	47·6
	2 g. fibrin. Digestion 2·75 hours.	
5.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	5·2
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	18·9
	1·7 g. fibrin. Digestion 1·25 hours.	
6.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	4·8
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	13·3
	1 g. fibrin. Digestion 2 hours.	

		Digestion in cc. of N/10 nitrogen
7.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl	8·9
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	22·7
	1·1 g. fibrin. Digestion 1·5 hours.	
8.	1 cc. pepsin, 10 cc. trypsin, 20 cc. water, 30 cc. N/10 HCl	7·2
	1 cc. pepsin, 20 cc. trypsin, 10 cc. water, 30 cc. N/10 HCl	5·1
	1 cc. pepsin, 30 cc. trypsin, 30 cc. N/10 HCl	4·2
	1 cc. pepsin, 30 cc. water, 30 cc. N/10 HCl	18·5
	1·8 g. fibrin. Digestion 1·5 hours.	

Of these experiments Nos. 1 to 4 were carried out with Benger's preparations, the others being with Merck's pepsin and trypsin (1 % solutions). As Liquor Pancreaticus is slightly acid, it was first neutralised, and a corresponding small amount of sodium chloride added to the control flask though this was probably not at all necessary.

It may be mentioned that exactly similar results were obtained by using Grübler's pepsin and trypsin in 1 % solution, and that many other experiments carried out with Benger's and Merck's preparations confirmed in every respect those described above, but those quoted are sufficient to show very clearly the effect of an excess of trypsin in inhibiting the digestive action of pepsin solutions. Experiments 4 and 8 also show that this inhibition varies with the proportion of trypsin present. If the amount of the latter enzyme be very large, the action of the pepsin is almost stopped entirely. This is what was to be expected if we assume that trypsin can combine with protein in acid solution.

The objection might be raised that the action of the trypsin was really due to the presence of protein or the products of protein digestion in the trypsin solutions used. That such is not the case, however, is shown by the following experiments.

		Digestion in cc. of N/10 nitrogen
9.	1 cc. pepsin, 20 cc. 2·5 % albumin, 30 cc. N/10 HCl	26·3
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	25·4
	1 g. fibrin. Digestion 1·5 hours.	
10.	1 cc. pepsin, 20 cc. 2 % caseinogen, 20 cc. water, 10 cc. N/10 HCl	29·7
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	24·9
	1 g. fibrin. Digestion 2 hours.	
	(The caseinogen was dissolved in N/10 HCl.)	
11.	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	31·9
	1 cc. pepsin, 20 cc. water, 30 cc. caseinogen	30·7
	1 cc. pepsin, 20 cc. water, 30 cc. albumin	37·6
	(The caseinogen and albumin were 1·5 % in N/10 HCl.)	
	1·2 g. fibrin. Digestion 1 hour.	

In these three experiments Liquor Pepticus was used.

		Digestion in cc. of N/10 nitrogen
12.	1 cc. pepsin, 20 cc. water, 20 cc. N/10 HCl	25·8
	1 cc. pepsin, 20 cc. water, 20 cc. caseinogen	24·4
	1 cc. pepsin, 20 cc. water, 20 cc. albumin	26·1
	1·1 g. fibrin. Digestion 1·75 hours.	
	(The caseinogen and albumin were 1 °/₀ in N/10 HCl.)	

Merck's pepsin (0·1 °/₀) was used in this experiment.

13.	1 cc. pepsin, 20 cc. water, 20 cc. N/10 HCl	32·3
	1 cc. pepsin, 20 cc. water, 20 cc. caseinogen	32·6
	1 cc. pepsin, 20 cc. water, 20 cc. albumin	31·7
	1·2 g. fibrin. Digestion 0·75 hour.	
	(Caseinogen and albumin 1 °/₀ in N/10 HCl.)	

Grübler's pepsin (1 °/₀) was used in this experiment.

It is clear from these experiments that digestion of a solid protein such as fibrin is not less rapid when there is also present in solution a protein such as caseinogen or egg albumin. The action of the pepsin on the fibrin seems to begin immediately in such a case, there being no interval during which the protein in solution is first broken down into less complex substances.

The action of the trypsin is not an actual destruction of the pepsin. This is at once seen if the amounts of fibrin used vary considerably. It has been shown by Hedin [1905] that the amount of caseinogen digested in a given time by a certain amount of trypsin increases with the concentration of the substrate, until a maximum is reached when sufficient substrate is present to unite with the whole of the trypsin.

Similar results are obtained in the digestion of fibrin by pepsin.

		Digestion in cc. of N/10 nitrogen
14.	1 cc. pepsin, 20 cc. trypsin, 20 cc. N/10 HCl, 0·9 g. fibrin	9·9
	1 cc. pepsin, 20 cc. trypsin, 20 cc. N/10 HCl, 2·7 g. fibrin	28·8
	1 cc. pepsin, 20 cc. water, 20 cc. N/10 HCl, 0·9 g. fibrin...	20·7
	1 cc. pepsin, 20 cc. water, 20 cc. N/10 HCl, 2·7 g. fibrin...	65·6
	Digestion 1 hour.	
15.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl, 0·9 g. fibrin	10·9
	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl, 3·4 g. fibrin	42·2
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl, 0·9 g. fibrin...	25·5
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl, 3·4 g. fibrin...	94·1
	Digestion 0·75 hour.	

In these two experiments Benger's preparations were used.

16.	0·8 cc. pepsin, 25 cc. trypsin, 30 cc. N/10 HCl, 1 g. fibrin	7·9
	(*a*) 0·8 cc. pepsin, 25 cc. trypsin, 30 cc. N/10 HCl, 3·5 g. fibrin	17·1
	(*b*) 0·8 cc. pepsin, 25 cc. water, 30 cc. N/10 HCl, 1 g. fibrin	22·4
	0·8 cc. pepsin, 25 cc. water, 30 cc. N/10 HCl, 3·5 g. fibrin	84·5
	Digestion 0·75 hour.	
17.	0·8 cc. pepsin, 25 cc. trypsin, 30 cc. N/10 HCl, 0·7 g. fibrin	4·9
	(*a*) 0·8 cc. pepsin, 25 cc. trypsin, 30 cc. N/10 HCl, 5 g. fibrin	12·7
	(*b*) 0·8 cc. pepsin, 25 cc. water, 30 cc. N/10 HCl, 0·7 g. fibrin	18·5
	0·8 cc. pepsin, 25 cc. water, 30 cc. N/10 HCl, 5 g. fibrin...	121·9
	Digestion 0·75 hour.	

		Digestion in cc. of N/10 nitrogen
18.	0·8 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl, 0·5 g. fibrin	4·7
	0·8 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl, 1·5 g. fibrin	12·6
	0·8 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl, 7 g. fibrin	13·1
	0·8 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl, 0·5 g. fibrin	10·5
	Digestion 0·5 hour.	

0·5 % pepsin and 1 % trypsin (Grübler) were used in these three experiments.

Those experiments show well the effect of varying the quantity of fibrin added to the enzyme solutions. It is clear that the effect of adding an excess of trypsin to a given amount of pepsin can be apparently counteracted by increasing the amount of fibrin. The reason evidently is that when the fibrin is increased in amount a larger number of pepsin molecules can carry on their digestive action, although in those experiments at least the amount of digestion by pepsin + trypsin relative to that by pepsin alone is no greater when much fibrin is present than when a smaller amount of the substrate only is used.

In experiments 16 and 17 it will be noticed that the amount of digestion in (*a*) is still less than that in (*b*) in spite of the fact that the amount of fibrin in the former is considerably greater than in the latter case. In these two experiments the proportion of trypsin to pepsin is probably higher than in experiments 14 and 15, consequently the proportion of fibrin should have been correspondingly higher in (*a*) than in (*b*) to produce the same effect. By using still smaller amounts of fibrin as in No. 18 this difficulty is got over, and in this last experiment we see again that by employing suitable proportions of fibrin it is possible to get a greater amount of digestion by the pepsin + trypsin than by the pepsin alone.

Since it has been clearly shown that the inhibition of pepsin by excess of trypsin is not due to the presence of soluble protein in the trypsin solution, also that it is not due to the pepsin being destroyed by the trypsin, it seems reasonable to suppose that this inhibition is due to the trypsin itself. If this were the case, we should expect that such an inhibition would no longer occur if the trypsin were destroyed.

The simplest way appeared to be by boiling the solution of trypsin before adding it to the pepsin. This, however, proved somewhat ineffective as the following show.

		Digestion in cc. of N/10 nitrogen
19.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl... ...	9·9
	1 cc. pepsin, 20 cc. boiled trypsin, 30 cc. N/10 HCl ...	16·8
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	28·8
	1·6 g. fibrin. Digestion 2·25 hours.	
20.	1 cc. pepsin, 20 cc. trypsin, 30 cc. N/10 HCl... ...	15·4
	1 cc. pepsin, 20 cc. boiled trypsin, 30 cc. N/10 HCl ...	20·7
	1 cc. pepsin, 20 cc. water, 30 cc. N/10 HCl	40·2
	1·7 g. fibrin. Digestion 1·5 hours.	

In these two experiments Liquor Pepticus and Liquor Pancreaticus were used. The latter was boiled under a reflux condenser for about 30 minutes and filtered. The precipitate was found to be entirely and readily soluble in the same concentration of pepsin as was used for the main experiment. As mentioned in a previous paper by me [1914] this trypsin preparation is slightly acid and retains a considerable proportion of its digestive power even after being boiled. In the last two experiments therefore, the digestive power of the trypsin was probably not entirely destroyed, or at least the power of the trypsin to unite with its substrate. In this case it is easy to understand why boiled trypsin still inhibits the action of pepsin on fibrin.

It may be mentioned here that it was through these unexpected results that I was led to investigate the effect of heat on trypsin more fully. As it has been shown in the paper referred to and by other workers that trypsin loses its digestive power readily when boiled in neutral or alkaline solution, I tried the effect of trypsin, which had been thus boiled, on pepsin, but found that it was still effective in inhibiting the digestion of fibrin by pepsin.

There is reason to believe, from preliminary experiments, that it is much harder completely to inactivate the trypsin molecule than the pepsin molecule, so that the zymoid modification of trypsin would still inhibit the action of pepsin even after prolonged heating of the trypsin solution. Different trypsin preparations also are found to behave differently in this respect. It was also found by Bearn and Cramer that different preparations of pepsin varied considerably in their behaviour to heat. The results with trypsin will be described in a later paper on this subject.

Trypsin was found to inhibit the action of pepsin on caseinogen solutions also, but the effect of pepsin on this substrate is slight, so far, at least, as rendering the nitrogen non-precipitable by tannic acid goes.

		Digestion in cc. of N/10 nitrogen not ppted. by tannic acid
21.	1 cc. pepsin, 20 cc. trypsin, 15 cc. N/10 HCl... ...	3·1
	1 cc. pepsin, 20 cc. water, 15 cc. N/10 HCl	6·2
	20 cc. of 1 % caseinogen in N/20 HCl added. Digestion 4 hours.	
22.	1 cc. pepsin, 20 cc. trypsin, 30 cc. 2 % caseinogen in N/10 HCl	9·8
	1 cc. pepsin, 20 cc. water, 30 cc. 2 % caseinogen in N/10 HCl	14·3

Liquor Pepticus and Liquor Pancreaticus used in these two experiments.

In No. 22, digestion lasted 18 hours, so that while these experiments show that trypsin again inhibits pepsin, they show still more clearly that this method is unsuitable for estimating the digestive activity of pepsin solutions.

EFFECT OF EXCESS OF PEPSIN ON THE DIGESTIVE ACTION OF TRYPSIN.

The experiments were carried out similarly to those already described. When Liquor Pepticus was used as the pepsin solution, a considerable allowance had to be made for the acidity of this solution, the control solution having sodium chloride added in amount corresponding to that in the neutralised pepsin solution.

		Digestion in cc. of N/10 nitrogen
23.	1 cc. trypsin, 20 cc. pepsin, 40 cc. 1 % Na_2CO_3	6·7
	1 cc. trypsin, 20 cc. water, 40 cc. 1 % Na_2CO_3	12·2
	1 g. fibrin. Digestion 2 hours.	
24.	1 cc. trypsin, 20 cc. pepsin, 40 cc. 1 % Na_2CO_3	7·9
	1 cc. trypsin, 20 cc. water, 40 cc. 1 % Na_2CO_3	18·6
	1·2 g. fibrin. Digestion 2 hours.	
25.	1 cc. trypsin, 10 cc. pepsin, 20 cc. water, 35 cc. 1 % Na_2CO_3	26·4
	1 cc. trypsin, 20 cc. pepsin, 10 cc. water, 35 cc. 1 % Na_2CO_3	21·1
	1 cc. trypsin, 30 cc. pepsin, 35 cc. 1 % Na_2CO_3	12·8
	1 cc. trypsin, 30 cc. water, 35 cc. 1 % Na_2CO_3	33·3
	2 g. fibrin. Digestion 1·5 hours.	

Liquor Pancreaticus and Liquor Pepticus were used in these experiments.

It will be seen from the above that an excess of pepsin inhibits the action of trypsin on fibrin, the amount of inhibition varying with the amount of pepsin added.

On the whole it was found that much more digestion was effected when caseinogen was used as the substrate, and the nitrogen estimated in the filtrate from the tannic acid precipitate.

		Digestion in cc. of N/10 nitrogen not ppted. by tannic acid
26.	1 cc. trypsin, 20 cc. pepsin, 40 cc. caseinogen	20·3
	1 cc. trypsin, 20 cc. water, 40 cc. caseinogen	46·9
	Caseinogen was 2 % in 1 % Na_2CO_3. Digestion 3 hours.	
27.	1 cc. trypsin, 20 cc. pepsin, 40 cc. caseinogen	28·2
	1 cc. trypsin, 20 cc. water, 40 cc. caseinogen	53·6
	Caseinogen as above. Digestion 4 hours.	

The effect of a soluble protein such as caseinogen on the digestion of fibrin by trypsin was tested by two experiments.

		Digestion in cc. of N/10 nitrogen
28.	1 cc. trypsin, 20 cc. caseinogen, 20 cc. N/10 Na_2CO_3	19·3
	1 cc. trypsin, 40 cc. N/10 Na_2CO_3	16·3
	1 g. fibrin. Digestion 2 hours.	
	The caseinogen was 2 % in N/10 Na_2CO_3.	
29.	1 cc. trypsin, 20 cc. caseinogen, 20 cc. N/10 Na_2CO_3	17·9
	1 cc. trypsin, 40 cc. N/10 Na_2CO_3	16·8
	0·8 fibrin. Digestion 2 hours.	
	The caseinogen was 2 % in N/10 Na_2CO_3.	

These two experiments show that the presence of excess of a soluble protein such as caseinogen does not delay the digestion of fibrin by trypsin. Egg albumin, as is well known, inhibits the action of trypsin, and I found that only a small amount of fibrin was digested if albumin was added in place of the caseinogen in these two experiments. The above results show, however, that the inhibition of trypsin by excess of pepsin is not due to the trypsin digesting the proteins in solution before attacking the fibrin.

Several experiments were carried out to see if pepsin solutions which had been boiled lost their power of inhibiting the action of trypsin. Here again, as in the corresponding experiments with boiled trypsin in excess acting on pepsin, the results varied considerably.

		Digestion in cc. of N/10 nitrogen not ppted. by tannic acid
30.	1 cc. trypsin, 20 cc. pepsin, 40 cc. caseinogen ...	14·9
	1 cc. trypsin, 20 cc. boiled pepsin, 40 cc. caseinogen ...	40·3
	1 cc. trypsin, 20 cc. water, 40 cc. caseinogen ...	52·8

The caseinogen was 2 $^0/_0$ in N/10 Na_2CO_3. Digestion 3 hours.

Liquor Pepticus and Liquor Pancreaticus were used in this experiment.

This shows that pepsin by being boiled loses most of its power to inhibit trypsin. In this case the pepsin had been boiled for about 10 minutes. Probably it still retained some of its zymoid properties, which would have been destroyed by more prolonged heating.

Although I had previously noticed that boiled trypsin still inhibited the action of pepsin, it was in the course of this last experiment that I found, in one of the controls containing boiled trypsin and caseinogen, that the boiled enzyme had brought about a considerable amount of digestion of the protein. I was led from that to consider the question of the resistance of trypsin to heat, and since then have been unable to get clear evidence of the destruction of the inhibitory power of pepsin by heat. As was shown by Bearn and Cramer, different preparations of pepsin vary widely in their resistance to heat, and it may be that in my experiments the solutions have always retained their power of combining with the substrate. This question is being now investigated, and the results will be published in a later paper.

It may be mentioned that Bayliss found that he could not always produce the zymoid modification of trypsin, or at least demonstrate the action of the zymoid, and it is evident from the experiments described in this preliminary paper that a number of points have still to be settled in regard to the varying behaviour of different enzyme solutions after being heated.

SUMMARY.

Excess of trypsin inhibits the digestive action of pepsin in acid solution. Such inhibition is not due simply to the presence of protein associated with the trypsin. Nor is it due to the pepsin being destroyed by the trypsin.

The power of trypsin to inhibit pepsin is to some extent lost if the trypsin solution is boiled before being added to the pepsin.

It is suggested that trypsin can combine with protein in acid solution, so that although unable to digest such protein, an excess of trypsin would prevent pepsin from combining fully with the protein.

Similarly an excess of pepsin inhibits the digestive action of trypsin in alkaline solution. The amount of inhibition in this case is usually less than that caused by an excess of trypsin on the digestive power of pepsin in acid solution.

This inhibition again is not simply due to the presence of protein associated with the pepsin. Heating the pepsin solution destroys to a considerable extent its power to inhibit trypsin.

In this case it is suggested that the pepsin acts by combining with the protein in alkaline solution, thus preventing the digestion of the protein by the trypsin.

In both cases the amount of inhibition produced depends on the relative proportions of the enzymes present. Thus, the greater the amount of pepsin, the less digestion will be effected by a given amount of trypsin acting in alkaline solution.

REFERENCES.

Bayliss (1904), *Arch. Sci. Biol.* **11**, *Supplement*, 261.
Bearn and Cramer (1907), *Biochem. J.* **2**, 174.
Edie (1914), *Biochem. J.* **8**, 84.
Engesser (1880), *Maly's Jahresbericht*, 297.
Hedin (1903), *J. Physiol.* **30**, 155.
—— (1905), *J. Physiol.* **32**, 468.
Kühne (1876), *Maly's Jahresbericht.*
Langley (1881), *J. Physiol.* **3**, 246.
Pollak (1905), *Beiträge*, **6**, 95.
Schwartz (1905), *Beiträge*, **6**, 524.
Wróblewski, Bednarski and Wojczynski (1901), *Beiträge*, **1**, 289.

Reprinted from the BRITISH MEDICAL JOURNAL, *September, 19th, 1914.*

CARDIAC FIBRILLATION AND ITS RELATION TO CHLOROFORM ANAESTHESIA.

Being a Paper read in the Section of Anatomy and Physiology at the Annual Meeting of the British Medical Association, Aberdeen, July, 1914.

By Professor J. A. MACWILLIAM, M.D.

So long ago as 1887 I advanced the view that many cases of sudden death depending on cardiac failure are due to the sudden occurrence of fibrillation in the ventricles, the function of the cardiac pump being thus destroyed. Evidence was adduced to show the inadequacy of the current view of syncope to account for the facts in many instances of sudden dissolution, by the assumption of a sudden failure of the heart to contract, and the strong probability of the true cause lying, not in an abrupt enfeeblement or paralysis of the contractile power, but in the supervention of the useless and disastrous form of inco-ordinated activity known as "fibrillar contraction" or "fibrillation." In a paper in the BRITISH MEDICAL JOURNAL I urged the probability of this explanation as applying to various conditions in which sudden death occurs.[5] But the gulf between experimental physiology and practical medicine in this branch of study was vastly wider then than it is now, thanks, above all, to the labours of James Mackenzie and his followers. In recent years the view I propounded in 1887 has been adopted by Gibson, Mackenzie, and others, and evidence corroborating it has been brought forward by Hering.[1]

Former Observations.

At the time of my old papers, and for some years afterwards, the central question in regard to chloroform was that of respiratory failure *versus* primary cardiac failure, or rather the possible occurrence of primary cardiac failure, it being admitted that respiratory failure is the usual one when chloroform is steadily pushed to a toxic stage. My conclusion was an emphatic affirmation of the occurrence of primary cardiac failure as a form of chloroform collapse, in opposition to the conclusions of the Hyderabad Commission and other observers. Fibrillation had often been noted in the course of my experiments, especially as a result of the sudden intake of strong chloroform vapour, but I was not at that time satisfied as to its occurring in the absence of at least a temporarily excessive intake of chloroform. There was no evidence to warrant the assumption that such a mode of cardiac failure was an operative one in the administration of chloroform in the ordinary way in healthy animals, meaning by the latter phrase the *continuous* administration of the anaesthetic by the animal being put in a box* with chloroform, and allowed to inhale the vapour until complete anaesthesia is induced.

That with such continuous administration there is immunity from collapse due to fibrillation is a conclusion I wish to reaffirm to-day in view of experience spread over nearly thirty years. But when one comes to review the results of irregular or intermittent administration a very different tale has to be told—a tale of trouble and disaster that in the case of laboratory experimentation has given chloroform a bad reputation as compared with other anaesthetic agents, and has led to its falling into comparative disuse.

Further Evidence.

In the course of the last twenty years we have in this laboratory had entirely conclusive evidence of the liability to cardiac failure of this sort, especially in cats, in what is clearly a condition of light anaesthesia, while the conjunctival reflex may be distinctly present, and a tendency to reflex movements in response to afferent impulses very marked. In a series of sixteen cats, examined a year or two ago in conjunction with Dr. G. Spencer Melvin, intermittent administration of chloroform was employed, and collapse clearly due to fibrillation occurred in nine of the sixteen animals.

It is clear that in the case of the ordinary (healthy) laboratory animals, and especially in the cat, the exclusion of collapse from ventricular fibrillation would render chloroform, when used with reasonable care, a safe anaesthetic.

It is perfectly practicable to readminister chloroform again and again, using due care, without inducing fibrillation, while a sudden readministration or a sudden increase in the strength of the vapour inhaled during the sensitive stage may readily induce collapse from fibrillation. In this respect the use of mixtures of air and chloroform of known strength offers obvious advantages.

In some exceptional instances (cats) so excessively sensitive a cardiac condition may be developed, after lightening of the original anaesthesia, that recommencement of the inhalation of even low percentages of chloroform is apt to be attended by the speedy occurrence of fibrillation.

It may be noted that the hypodermic administration of such drugs as omnopon and chloral, while assisting the development of anaesthesia, do not afford any protection against chloroform fibrillation, if they do not, indeed, make the heart more prone to fibrillate; in any case, they tend towards the prolongation of the stage of insufficient chloroform which is associated with the liability to fibrillation.

---

* Analyses recently made by Mr. E. S. Edie of the air in the box as regards O and CO_2 at the end of the induction of anaesthesia showed quite trivial differences.

Some Relations of Ventricular Fibrillation.

Ventricular fibrillation may occur at two phases of the action of chloroform: (1) In the early stage, this being by far the more common case; or (2) at a very advanced stage of the toxic action of the drug when the heart is greatly enfeebled and dilated. In some kinds of animals fibrillation may occur with great regularity as soon as the chloroform is pushed to a certain extent, weakening and dilating the heart.

Dilatation of the heart is not necessarily protective against the onset of fibrillation. Dilatation depends on diminished contraction—force and tone, while insensitiveness to fibrillation depends solely on a quite distinct condition—depression of excitability—which may or may not be associated with dilatation. Enfeeblement and diminution of tone are certainly often associated with dulling of excitability, but not necessarily so. There are cases of diminished sensibility associated with no sign of dilatation, and, on the other hand, marked proneness to fibrillation with marked dilatation.

The special incidence of chloroform fibrillation on the ventricles as compared with the auricles is noteworthy. The latter commonly preserve their rhythmic action, though they sometimes may fibrillate also.

There are some animals that seem to be specially liable to fibrillation under chloroform. In them we have very often found great resistance to the induction of anaesthesia, a very large amount of chloroform being required; during the induction marked excitability and tendency to struggle, quick irregular pulse, high blood pressure and defective vagus control over the heart. The complex and striking irregularity of the heart beat in cats in the earlier phases of chloroform administration attracted my attention very many years ago, and are mentioned in a paper in 1899.[5] These irregularities have recently been carefully studied by Lewis and Levy,[3] and their electrocardiographic features elucidated. It must be noted, however, that all the above-mentioned peculiarities in the behaviour of the animal may be present in a very marked degree without fibrillation occurring, and, on the other hand, an animal may go under the anaesthetic quite readily and quietly, to succumb to fibrillation at a later stage when the anaesthesia has become a light one, and there has been a recommencement or increased administration of chloroform by inhalation, especially (but not necessarily) of strong vapour, or the excitation of afferent impulses by some other cause. The onset of fibrillation is, as a rule, preceded by the development of complex irregularities.

Influence of the Vagus Control.

The relation of tonic vagus control over the heart is very important in this connexion. With normal or increased vagus tone the tendency to irregularity under chloroform is checked and fibrillation prevented.* Sudden diminution or removal of vagus tone, like cessation of (artificial) vagus stimulation, is sometimes associated with the sudden development of fibrillation. In this way variations in the activity of the vagus centre during chloroform administration, under the influence of afferent impulses (for example, operative interference during insufficient anaesthesia), constitute an element of danger in cases where fibrillation is in question. In another way also, under similar conditions, vagus slowing followed by acceleration, causing marked alterations in the blood flow, and usually associated with disturbances of the respiration —temporary arrest followed by rapid exaggerated breathing—has the undesirable effect of interfering with the steady intake of the anaesthetic, and giving effects in some degree resembling those of an intermittent or irregular supply of vapour from without.

It is in such ways that the vagus plays an important part, not in the way of causing a permanent arrest of the heart by reflex inhibition. For the latter view no shred of evidence has been found in our long series of observations; it may be set aside as quite destitute of foundation. Serious depression of cardiac efficiency by continued central stimulation (for example, excitation of the vagus centre by chloroform) has found only very rarely any illustration in our experience; in only one or two cases was much good done by removal of the vagus influence (by section of both vagi). These conclusions apply to animals (cats especially) anaesthetized with chloroform alone, no morphine or other drug being used.

The Acapnia Hypothesis.

The variety of ways in which fibrillation may be provoked under chloroform tempts one to look for some common factor beyond the tolerably obvious condition of increased irritability. The condition of acapnia, depending on an abnormal diminution of the CO_2 of the blood, suggested by Yandell Henderson[2] as a very important factor or the chief factor in chloroform collapse, naturally comes under consideration. But the production of respiratory failure is what he emphasizes, whereas our experience has left no room for doubt that the failure in early chloroform collapse is primarily cardiac. In a series of cats referred to by Henderson there was nothing to show what was happening in the heart at the onset of collapse. We are not able to find anything in the acapnia hypothesis at all adequate to meet the facts observed by us.

---

* This is quite a different matter from the question of vagus influence on fibrillation once it has occurred. Vagus stimulation fails to *arrest* fibrillation.

Recent Investigations.

The conditions associated with ventricular fibrillation under chloroform have been investigated on an extended scale by Levy[4] in recent years, and with the majority, though not with the whole, of his conclusions as applied to animals our results in this laboratory are in general agreement. The same worker has developed a comparison between the features of early collapse in cats and in man, bringing out a striking similarity in the essential features in both cases.

Experiments on Animals and Anaesthesia in Man.

In attempting to correlate these results of animal experiment with what occurs in the human subject, it must be remembered that the results described above were obtained from animals for the most part healthy, as contrasted with the various morbid conditions present in the human subjects of anaesthesia. On the other hand, there is evidence that the proneness of the cardiac muscle to fall into fibrillation is greatly augmented in certain morbid conditions; the influence of disease may tell in one direction or the other, as seen in diseased animals.

The higher nervous organization and mental development of man have often been invoked as considerations in connexion with the action of chloroform, but it is important to note that the fatality of chloroform in the instances under consideration essentially depends on its action on fundamental vital functions of the vascular and respiratory systems, and not on the higher developments of the central nervous system.

Further, it is necessary to bear in mind the extraordinary sensitiveness in this respect—as regards liability to fibrillation under the influence of chloroform—in such an animal as the cat. Unquestionably the susceptibility of the latter is enormously greater than in man, otherwise the death-roll from chloroform would, under certain conditions, be an appalling one, such as would render the use of chloroform prohibitive.

It is to be noted that all the ordinary laboratory animals do not by any means (for example, the rabbit) show the same height of susceptibility as the cat. In the rabbit there may be pretty sudden cardiac failure with enfeeblement and dilatation of the heart, the rhythmic contractions persisting but being very inefficient. Such a form of failure may occur in the cat, but in the light of our evidence it is a rare form in this animal. In view of all the facts one would naturally exercise much caution in applying the results of animal experiments. At the same time there may be a susceptibility to fibrillation in the human heart essentially similar in nature to that present in the cat, though immensely less in degree, and the study of the striking and easily verified phenomena of the cat's heart may afford a clue to the hidden accidents of chloroform anaesthesia in the human heart.

The essential features of fibrillation and the general conditions favouring and determining its occurrence are so strikingly constant in all the warm-blood animals examined that there is no warrant for assuming an exception in man, but, on the contrary, a strong presumption in favour of a broad similarity in the essential nature of its behaviour in man and in mammals and birds.

Further, there is the striking resemblance between the general features antecedent to or associated with early collapse in the cat and in many recorded instances in man —tendency to excitement and struggling, with disturbance of respiration (holding the breath, exaggerated breathing, etc.). There is also a remarkable resemblance between the recorded phenomena of many cases of early collapse seen in man and those observable in the cat.

The conclusion is warranted that ventricular fibrillation is certainly the chief cause of early chloroform collapse in the cat, and is probably a very important cause of early chloroform collapse in man. No other explanation meets the facts so well as regards many such recorded cases in man; indeed, there is no other hypothesis that stands on any secure foundation.

REFERENCES.

[1] Hering, *Muench. med. Woch.*, 1912, Nos. 14 and 15. [2] Henderson and Scarbrough, *Amer. Journ. Physiol.*, 1910, xxvi, p. 260. [3] Lewis and Levy, *Heart*, 1911, iii, 99. [4] Levy, *Heart*, 1913, iv, 319; *Heart*, 1914, v, 299. [5] MacWilliam, BRITISH MEDICAL JOURNAL, January 5th, 1889; ibid., October 11th, 18th, and 25th, 1890; *Journ. of Physiol.* 1899 xxv., 233.

SOME OBSERVATIONS ON BLOOD PRESSURE.

BY

G. Spencer Melvin, M.D., and J. R. Murray, M.D.

Recent advances in methods of estimating blood pressure have given a great impetus to the study of the subject. It would seem desirable, therefore, to review the methods now available. A recognition of the importance of a knowledge of diastolic pressure and of pulse pressure has made it essential to consider as methods of blood-pressure estimation only such as permit of the determination of these pressures.

Of such methods two have been prominently advanced, and one, at all events, has been considerably utilized. The two methods are the maximum oscillation method and the auditory method. An extended study of these two methods has enabled us to appreciate the value and the defects associated with one or other method, and we propose to bring forward such points as determine in our own minds our adherence to one of the methods. In the application of the oscillation method we have made use of two instruments: (*a*) the Erlanger sphygmomanometer, which yields a graphic record, and (*b*) the Pachon sphygmo-oscillometer, in which the oscillations are examined by visual inspection. As index of systolic pressure we adopted that known as the Recklinghausen-Erlanger index—namely, the pressure corresponding to the point at which, with falling external pressure, there is an appreciable increase in the magnitude of the oscillations. With regard to the estimation of diastolic pressure, we have departed from the index suggested and employed by Erlanger. Prolonged investigation with an experimental schema convinced us that diastolic pressure was to be read at a lower level, and from the results brought forward in that experimental study we decided to adopt as the index of diastolic pressure the pressure corresponding with the point on the record at which, with diminishing external pressure, the oscillations showed an appreciable diminution in magnitude.

The indices of systolic and of diastolic pressures with the auditory method are very definite. Systolic pressure is clearly determined by noting the pressure at which the first sound is heard. Diastolic pressure is as clearly indicated by the pressure at the point at which the sound becomes diminished in intensity and duller in character—at the beginning of the fourth phase as it is called. For the present we will omit discussion of the controversy that has centred round the acceptance of this as the diastolic index.

Our method of study consisted in the concurrent application of these two methods in a large number of cases, and in the correlation of the results obtained from each. Roughly, two classes of individuals were examined—first, a set of healthy young adults of average age 20.9—a series we have nominated as "normals"; and secondly, a series of old people and of patients manifesting pathological conditions of circulation—a class we have nominated as "pathological."

In the "normal" series we examined 59 cases, and in all were able to make some determination of diastolic index from the tracing obtained by the Erlanger apparatus. In 19 cases, that is, 31 per cent., however, there was a discrepancy amounting to 10 or more millimetres between the oscillation and the auditory readings. Yet the average diastolic pressure of these 59 cases differed by the two methods by only 2.3 mm. Were the Erlanger index of diastolic pressure to be taken—that is, the reading corresponding with the last stage at which the oscillations are maximal—then the averages differed by 12.6 mm., with the oscillation reading higher than the auditory. In such cases as there occurred a marked difference between the oscillation and the auditory readings we accepted the latter, and for these reasons: At the systolic level similar differences frequently obtained, but at this point the pressure estimated by the tactile method confirmed the auditory reading. There is thus a suggestion of unreliability imparted to the oscillation method. The teaching of the experimental schema is decidedly in favour of the auditory indications being the more definite. Again, direct experiment on animals, in which the actual pressures obtaining were accurately determined and correlated with the readings concurrently obtained by the auditory method, proved conclusively the accuracy of the auditory method. Moreover, it is recognized that the oscillation magnitude depends on a complexity of conditions liable to great variation. We are thus led to accept as definite the readings obtained by the auditory method. The actual pressures which we regard as the normal pressures may then be given as follows: Systolic pressure normally amounts to 111.8, diastolic to 65.7, and pulse pressure to 46 mm. This estimate of diastolic pressure is decidedly lower than the values commonly given, and the estimate of pulse pressure correspondingly higher.

The average pulse rate was 80.1 per minute, but we failed to establish any definite relationship between the variations in the pulse rate and diastolic pressure level.

Taking the "pathological" series, there is at once apparent a striking difference. In consideration of the abnormal circulatory conditions prevailing, and the consequent influences affecting the changes in tranverse diameter and length of the artery with each pulse beat, there is to be expected an instability of the oscillation indications. So it is found. There is frequently great difficulty in making a reading of diastolic pressure from the tracing. There is frequent and serious discordance between readings thus made and the auditory reading. It may happen that the auditory and oscillation readings agree, but it just as frequently happens that they do not. In the latter case we have noted that the auditory reading may be correlated with a definite change in the tracing—a change other than that acceptable as the diastolic index, which itself, as a rule, then lies at a lower level. Again, we have noted the diastolic level indicated by the auditory method unrepresented in the tracing by any change at all distinctive. Here, as before, we accept the auditory indications. As the cases examined in this series yield a collection of pressure values in many varied conditions, there is little value in assessing averages. What we have done is to compare the ranges of variation of the different pressures with the corresponding ranges in the "normal" series. Thus, in the latter diastolic pressures from 82 to 50 were obtained, while in the "pathological" series, values from 150 to 50 were got. Similiarly, the range of variation of pulse pressure was respectively in the normal and the pathological series 73 to 22 and 163 to 26. There is thus a much greater range of variation in the pathological series.

This investigation we made brought out definitely a point of considerable importance in the application of the auditory method. In examining the "normal" series, we were struck by the remarkably low level of pressure to which the sound persisted. As we indicated earlier, this point is one of great moment. It has been suggested that the auditory index of diastolic pressure is the point at which all trace of the sound is lost—the lower limit of sound—the fifth phase. We early found, however, that between the beginning of the fourth phase—the true index, as we believed, of diastolic pressure—and the end of it there lay a wide and varying range of pressure.

We can select out of our 59 cases 14 in which the average duration of the fourth phase was 38.3 mm. The serious problem was that if we were to accept the lower limit of sound as the indication of diastolic pressure, we should have to assign to that pressure a normal value of 42.2, and to admit such incredible values in individual cases as 10, 14, 20, etc. We felt confirmed, therefore, in our acceptance of the fourth phase as the index of diastolic pressure. Further confirmation was obtained by animal experimentation previously referred to. We ascertained conclusively that the actual diastolic pressure within the artery of the animal was faithfully recorded by the distinct alteration in the sound characterizing the onset of the fourth phase, and that abolition of the sound came much later.

Now, duration of the fourth phase, variously estimated, has never been assigned such high values as we have given. It may be that light is shed on this discrepancy by results we ourselves have obtained in other series of investigations. In children, middle-aged and elderly persons in ordinary health, and in persons with thickened arteries, the fourth phase is extremely short; there is usually no serious or, indeed, appreciable error in taking the abolition of the sound as the diastolic reading, for such abolition almost immediately follows the dulling and weakening which constitutes the true diastolic index. It is in young adults that the danger of grave error becomes manifest. It is a curious fact that the occurrence of a long fourth phase should apparently be restricted, or almost restricted, to this period of life. This fact, we say, may explain the discordance between the results that have been obtained by ourselves and by other observers. Highly trained investigators have put the duration of the fourth phase at only a few millimetres, and have naturally regarded the abolition of the sound as being a sufficiently accurate guide. These observers have probably worked mainly with hospital cases and with middle-aged or old persons. It was only when we examined a series of normal young adults that we became impressed with the great variability and frequently long duration of the fourth phase.

We advance its simplicity, accuracy, and applicability as reasons for the adoption of the auditory method as the most satisfactory method of blood-pressure estimation.

Reprinted from the BRITISH MEDICAL JOURNAL, *November 7th, 1914.*

SOME OBSERVATIONS ON THE SIGNIFICANCE OF BLOOD-PRESSURE READINGS IN MAN.

BY
J. A. MACWILLIAM, M.D.,
AND
G. SPENCER MELVIN, M.D.
(From the Physiological Laboratory.)

DIFFERENT opinions are held as regards the practical value of blood-pressure estimations in elucidating the actual conditions of the circulation. It may be stated with confidence that a single estimation of systolic or obliteration pressure, using the first reading obtained, is in some cases open to serious fallacy—apart altogether from psychical disturbances, etc.—even as an estimate of the maximum (systolic) pressure obtaining at that time in the artery under examination.

In former communications we urged the importance of using *continued* local pressure as an aid to correct estimation of the systolic pressure in certain abnormal conditions of the arterial system, an addition to the usual method.[4] [5]

But the systolic pressure, even if accurately gauged, gives very insufficient evidence as to what is going on in the circulation. For example, in cases of complete heart-block, where very high systolic readings may be obtained, the mean blood pressure is low and the blood flow is very defective, as shown in various ways, including manifestations of cerebral disturbance from cerebral anaemia, etc. Here the systolic estimation would fallaciously rate the "blood pressure" as being above normal. Again, in cases of slow cardiac failure the systolic pressure may be about the normal level, while the circulation is very inadequately carried on, as evidenced by obvious signs (cyanosis, dyspnoea, etc.).

Diastolic Pressure.

The importance of estimating the minimal or diastolic pressure is now becoming more generally recognized, and with the easy applicability of the auditory method there is no difficulty in the way of its routine use.

Apart from the influence of aortic diastolic pressure in determining (*a*) the strain upon the closed aortic valves, and (*b*) the resistance to the opening of these valves by the ventricular systole, the distending force of load which it imposes on the arterial tube is of prime importance. The properties of the arterial wall are such as to show relatively great effects from long-continued tension as compared with the transient application of distending force, as in the brief rises of pressure that constitute the systolic waves. Experiments upon excised surviving arteries demonstrate very strikingly the different degrees of yielding of the vascular wall in the two cases, especially in a tonically contracted artery.[3]

As long as the diastolic pressure remains low, even with very high systolic readings, the tendency to the giving way of vessels (cerebral haemorrhage, etc.) seems to be relatively slight—for example, in aortic regurgitation.

The greater proneness of the leg arteries to degeneration is especially associated, in all probability, with the high diastolic pressure in the erect position, rather than with the concomitant increase in the systolic level, which is also induced by the influence of gravity.

The evidence available at present is insufficient to show in what measure the injurious effects of an excessive diastolic pressure are to be attributed (*a*) to the influence of mechanical strain upon the tissue elements of the arterial wall, and (*b*) to the influence of a high distending pressure on the flow of blood and lymph in the walls of the arterial tube.

Much requires to be done to elucidate the relations of increased or diminished expansion, depending either on alterations in the tone of the arterial muscle or in variations in the intra-arterial pressure, on the blood flow in the capillaries of the vasa vasorum and on the lymph flow; also the relations of hypermyotrophy and atrophy of the media and hypertrophy of the intima to the intra-arterial pressure, as well as to the various toxic influences that are known to affect the nutrition of the vessels.

Is hypermyotrophy a response to increased internal pressure, comparable with some forms of cardiac hypertrophy developed in certain conditions? Is the diastolic pressure the one that is of primary importance in this connexion?

In regard to various conditions which may exercise a special influence on the diastolic pressure, variations in peripheral resistance are most important, a low diastolic pressure naturally resulting from defective peripheral resistance, and vice versa, unless the heart action is much altered. Apart from alteration in peripheral resistance, quickening of the heart rate *tends* to raise the diastolic pressure by diminishing the time for outflow through the periphery between the pulse beats, and the converse holds with a slowed heart; that is, the diastolic pressure is lowered, with an increase in the range between the systolic and diastolic levels (pulse pressure). It must not, however, be assumed that a slow pulse rate is necessarily associated with a low diastolic pressure. Compensating adjustment in the vascular mechanism often keeps the diastolic pressure quite up to a normal or even heightened level with a slow heart beat, in spite of the lowering tendency of the latter. And the diastolic pressure may be very low with a very quick heart beat, for example, with very defective peripheral resistance, lessened inflow into the heart, etc.

In doing blood-pressure estimations we find it desirable to determine the diastolic index while the armlet pressure is being raised; in some (rare) cases where arm compression leads to a marked rise of blood pressure, the diastolic reading taken with a rising armlet pressure may differ from that obtained during the lowering of the armlet pressure (after determining the systolic index) by as much as 20 mm. This was especially the case when simultaneous estimations were made in the two arms. But a decided effect was sometimes observed when only one arm was tested. Comparison of the diastolic values with rising and falling armlet pressures may thus give important indications of the liability of the arterial pressure to vary in an abnormal way, when a large artery is closed, as in the process of systolic estimation.

As regards the impressions derived from *digital* examination of the pulse, we have found the impression gained as to (*a*) the tension in the vessel within the beats (diastolic pressure), and (*b*) the extent of the change at systole (pulse pressure) to be specially fallacious in some cases—apparently more deceptive than the impression as to the compressibility of the pulse (systolic pressure). An enormous pulse pressure (for example, 120 mm. in a case of aortic regurgitation) may be present, as shown by measurement of the systolic and diastolic pressures, when the finger fails to give any adequate conception of such a pressure wave along the artery. And the measured diastolic pressure may be very high when the impression given by digital examination is that it is rather low.

Some Points in Relation to the Auditory Method.

In former papers we urged the importance of the auditory (auscultatory) method as a simple and accurate means of estimating the diastolic or minimum pressure as well as the systolic or maximum pressure, and our further experience of this method has entirely borne out all that we have said in this connexion.[5] It is clear that if the study of blood pressure is to be successfully applied to elucidate the circulatory conditions in man in health and disease, the examination must include routine estimation of systolic and diastolic pressures with computation of the pulse pressure; such estimation by the auditory method is easy and expeditious, and must replace the very inadequate procedure of systolic estimation alone, as well as the use of the oscillatory method for diastolic estimation.

The term "diastolic" pressure is used in the same sense as "minimum" pressure, to indicate the pressure at the deepest part of the trough between the systolic waves. Of course the arterial pressure varies much at different phases of the period of cardiac diastole, so that there are different levels of pressure at different points in the diastolic interval. The same applies to the period of systole. But, as by common consent the term "systolic pressure" is applied to the highest level resulting from the cardiac systole, so the term "diastolic" pressure designates the lowest point to which the pressure falls between the pulse-beats.

In regard to the *rationale* of the auditory method to the recognition of systolic pressure, no difficulty arises. But in regard to the use of this method for diastolic pressure estimation, the question may be raised as to how the sound produced in the systolic phase and depending upon the systole can serve as an index of diastolic pressure. The answer is that, though the sound is actually elicited by the systolic wave, its occurrence or non-occurrence and its character when present, are determined by the intra-arterial pressure existing during the diastolic phase and its relation to the external or armlet pressure. If the intra-arterial diastolic pressure stands in such a relation to the armlet pressure that some distortion of the arterial tube from the circular form—that is, some flattening—occurs during diastole, then the loud clear tone is heard. On the other hand, when the relation is such that the intra-arterial diastolic pressure is not sufficiently below the level of the armlet pressure to ensure some flattening between the pulse beats, the sound, if audible at all, is dull in character. The change (during the lowering of the armlet pressure) from the clear to the dull and weaker sound, occurring as soon as the external and internal pressures are approximately equal, constitutes the index of diastolic pressure. In addition to the lines of evidence (as to the correctness of this index) stated in our former papers (study of circulatory schema, comparison with oscillatory method, etc.), we may add the direct experimental test carried out by us in conjunction with Dr. J. R. Murray.[6] Using anaesthetized large animals (sheep), we measured the systolic and diastolic pressures in one carotid artery by means of valved manometers (maximum and minimum) connected with a cannula inserted into the artery at the root of the neck on the proximal (cardiac) side of an armlet which was placed round the neck. The armlet being inflated in the usual way, the actual intra-arterial pressures were read off by one observer on the valved manometers, while simultaneous estimations were made by the auditory method by another observer; the auditory tambour (phonendoscope) was placed over the other carotid on the distal side of the armlet. These simultaneous readings by different observers (changing places from time to time) showed remarkably close correspondence; the auditory indications proved a strikingly accurate guide to the actual intra-arterial pressures as measured by the valved manometers. Such observations were carried out while the levels of blood pressure (systolic and diastolic) were made to vary widely—raised by compression of the abdomen, lowered by amyl nitrite, excess of chloroform, etc., also at very different rates of heart beat, etc. In all such conditions the accuracy of the auditory indications remained unimpaired.

Relation of Systolic and Diastolic Values to Efficiency of Circulation.

When systolic and diastolic pressures have been estimated and found to be at normal or approximately normal levels, with a normal rate of heart-beat, is this sufficient to prove that the circulation is proceeding in normal fashion? In the great majority of cases presenting the normal features referred to, it is the case that the blood flow is proceeding normally. But there are exceptional conditions where, with normal systolic and diastolic pressures, the mass movement of the blood is gravely defective, and the results are evident in the patent signs of circulatory defect —dyspnoea, pallor, or lividity, etc. Though the pressures may be normal, the volume of the arterial stream may be abnormally small, giving rise to circulatory defect. A small output of the heart with a suitable adjustment of the peripheral resistance by constriction of arterioles (necessary to maintain the aortic pressure in presence of the small output of the left ventricle) may establish a condition in which normal or not far from normal pressure readings may be accompanied by very deficient mass movement of the blood. The circulation has in this case been reduced to a smaller size than is compatible with the needs of the animal. The arterial stream may be seriously lacking in volume while showing readings of systolic and diastolic pressure that are not far from normal. With such defective volume the capillary flow is seriously reduced on account of the deficient mass movement of the blood, the small cardiac output being associated with narrowing of the peripheral outlet from the excessive contraction of arterioles which is necessary to maintain the aortic pressure in presence of the small output of the left ventricle.

In children and in small animals the volume of the arterial stream is, of course, very small as compared with the adult man, while the normal relation of peripheral resistance is related to the cardiac output in such a way that the aortic pressures may be pretty similar. The latter pressures in the aorta being maintained without any undue constriction of arterioles, the capillary circulation is a perfectly efficient one, and the mass movement of the blood is rapid. The smaller volume of the arterial stream is adapted to the smaller capillary field to be supplied. With the enormously large capillary field of the adult person a great reduction in the volume of the arterial stream, even with pressures up to the normal, means a serious defect in the capillary stream and the mass movement of the blood in the circulation—hence, signs of circulatory inadequacy. On the other hand, the volume of the arterial stream may be normal, while the circulation is still inadequate; in this case a pressure defect will be evident—abnormally low systolic or diastolic readings or a small pulse pressure. With deficient pressure values a reduced volume of arterial stream would of course imply a still more serious deficiency in the circulation.

Common Readings in Defective Circulations.

The more common conditions, when the circulation is defective, are: (*a*) Low systolic and diastolic readings (as in haemorrhage, shock, etc.), or (*b*) a systolic pressure which may be normal or even higher, attended by an abnormally high level of diastolic pressure, as in some cases of slow cardiac failure. Here the peripheral resistance is increased, keeping up the systolic pressure, notwithstanding a poor cardiac output, but this involves a high diastolic pressure—that is, a small pulse pressure and associated defective movement of the blood. The rate of the heart beat has, of course, to be taken into account in connexion with the pulse pressure. The defective pulse pressure is here of great significance and at once shows the true state of the circulation, whereas the systolic reading taken alone would give an entirely false indication.

It is clear that estimation of the systolic and diastolic pressures with the concomitant determination of the pulse pressure yields data of great importance and value, the precise significance of which in different conditions will, no doubt, become much greater with increasing knowledge. But while this is the case, such estimations must on no account be regarded as superseding or rendering unnecessary the use of other sources of information regarding the condition of the circulation—for example, obvious signs such as pallor, lividity, defective volume of arterial pulse, venous turgescence, dyspnoea, etc. Error from misuse of the results of blood pressure estimation, by blind adherence to mechanical standards, is easily avoided by common-sense application of other obvious signs taken in correlation with the blood pressure data.

Discrepancies in Systolic Readings from Different Limbs.

In a former paper we described the occasional presence of large discrepancies between the systolic readings obtained from different limbs, apparently due to abnormal local conditions.* The higher readings may be greatly reduced by the application of continued local compression, as already described, and in this way the divergent readings may be harmonized, the same readings being then obtained from all the limbs; further local compression may then cause no further lowering of the systolic values. As already stated, it is only in *some* abnormal arteries that such results are obtained; in the majority of thickened arteries practically correct readings are obtained without the preliminary use of continued local compression. The effects of local compression are not dependent on the production of an ischaemic condition of the limb. The closure of the brachial artery—by digital pressure as employed—leads, of course, to more or less pronounced stasis in the limb, but not to ischaemia. The latter condition, induced by the application of an Esmarch bandage, was found by Hill[1] and his collaborators to lead to reduced systolic readings for some time after the obstruction to the arterial flow was removed. This holds good in a normal limb as well as under abnormal conditions.

---

* In this connexion we specifically exclude the cases of arm-leg differences associated with aortic regurgitation.

This observation deals with very different conditions from those present in the use of local compression. Local compression, as we employ it, leads to no alteration in the subsequent systolic reading either in normal persons or in the majority of pathological conditions. We have repeated this observation very frequently and with constant results. A pressure reading was first taken from the two arms. One arm was then subjected to repeated compression (for example, twenty times), or, as is preferable, closure of the brachial artery by digital pressure was maintained for three minutes in the area of application of the armlet, the latter being loosened and slipped down on to the forearm or removed altogether. At the end of the period of closure the armlet, reapplied to the upper arm, gave, in the normal subject, a reading which, when compared with one made from the other arm, showed no discrepancy. Comparison with a (second) reading from the other arm which has not been subjected to continued or frequently repeated compression is, of course, essential, as the actual pressure in the arterial system might have undergone some alteration during the period occupied in the observations. The procedure of local compression clearly induces no change in systolic readings in ordinary conditions of the vascular system; this is also true of the great majority of abnormal conditions.

It is only in a small minority of cases with thickened and contracted arteries that a notable reduction of the systolic reading is induced by local compression as described. We have not observed such reduction in any case where there was not evidence of abnormality in the arteries. In cases where divergent readings have been obtained from different limbs, local compression has an equalizing effect. Repetition of the local compression does not induce an indefinite reduction of the readings—not below the level found in a normal or soft artery.

Parallelism between Results from Excised Arteries and Human Limbs.

A long series of experiments (conducted in association with Dr. J. E. Kesson[4]) on excised arteries tested in different conditions in a circulatory schema showed a remarkable parallelism as regards the results of continued compression with those described above. With relaxed arteries (normal or thickened) the "systolic" reading was practically the same before and after continued compression, whereas with powerfully contracted and thickened arteries the subsequent reading was greatly reduced—down to the level of that obtained with relaxed vessels. The continued compression induced relaxation at the compressed part, as was evident on direct examination of the artery, which was soft and easily distensible at that part, in marked contrast to the firm and resistant adjoining parts which had not been subjected to compression. This reduction in the resistance of the arterial wall was temporary; after a time, varying according to circumstances, recovery occurred more or less completely; the contraction and resistance to compression returned, causing the external (obliteration) pressure to be again an over-estimate of the systolic pressure within the artery by the amount of the resistance to compression offered by the arterial wall. Similarly, in the human subject, when the systolic reading had been reduced by continued local compression of the thickened artery, recovery occurred after a time, and the original systolic value was restored; in some cases this restoration was watched and found to occur with remarkable precision in observations repeated from time to time on the same patient over a period of many months. But in most cases the extra resistance, as indicated by the result of local compression, varied considerably from time to time in the same person.

The striking resemblance in the results got from resistant excised arteries and those sometimes obtained from human limbs naturally suggested the possibility or probability of a similar explanation being applicable in the two cases. But it is to be noted that while the parallelism between the results from excised arteries and from the living subject is a perfectly definite and very striking one as regards the nature of the changes in pressure readings, the actual amounts of the alterations in the readings differ widely in the two classes of observations; in other words, there is a very close correspondence in the *kind* of change which occurs in each case, but a great difference in the *degree* of such change.

The alterations induced by continued compression in the human limb are, in some cases in which they are very extensive, very much greater in amount than could be predicated from the study of excised arteries. We have always borne this consideration in mind; in the first paper on the subject from this laboratory we adverted to this, and pointed out that it was impossible to account for the extensive variations in the systolic readings from different limbs sometimes met with, unless one assumed the existence of such enormous resistances as are to be met with in the powerfully contracted thick-walled arteries like the carotid of the ox or the metacarpal or metatarsal of the horse, examined under abnormal conditions calculated to give the maximum resistance, at room temperature, or under the influence of barium chloride, etc. Palpation of arteries in the living subjects under examination has not in our experience given evidence of such extremely resistant characters as were present in the excised arteries above referred to; we have never believed that the great differences in pressure readings in different limbs depended simply on the extra pressure required to distort the circular tube and bring it into a flattened position. There is, we believe, another factor which we have not so far described—resistance, due, as far as is known, to contraction of the arterial muscle acting in another way than simply by opposing the flattening of the circular tube, but in effect constituting a local resistance to the obliteration of the pulse in the artery compressed by the armlet; this depends on certain special features in the form of closure of the vessel when compressed by external pressure.

Resistance to Compression in Excised Arteries.

In an artery like the sheep's carotid, comparable in size and thickness of wall with the human brachial, contraction of moderate amount made very little difference to the pressure readings; this accords with evidence derived from other sources in showing that the normal tone of the brachial artery, and even a markedly increased tone, have no appreciable disturbing effect on blood pressure estimation. Even with extreme contraction, induced by mechanical stimulation at room temperature, use of barium chloride, etc., the resistance offered by the carotid of the sheep in these abnormal conditions, widely removed from those present in the human body—for example, 35 mm.—has not reached anything like the values sometimes observed in the differences between the human limbs in certain conditions (cases of aortic regurgitation are excluded). We conclude, then, that variations in the amount of contraction, such as occur in the normal brachial artery of man, are of no serious import in regard to blood-pressure estimation.

Janeway and Park[2] conclude that resistance of the arterial wall due to muscular contraction may be a source of error in blood-pressure estimations, so far supporting the view long held by Russell[8] to this effect. Janeway and Park think that such error should not be more than 30 mm. in the human brachial artery.

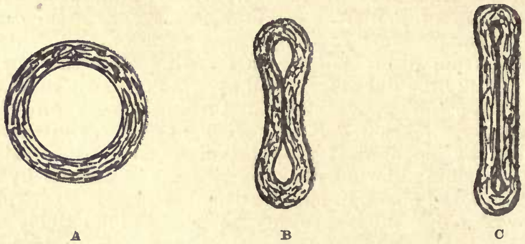
Higher resistance values were naturally obtained from such large thick-walled tubes as the carotid of the ox with its powerful muscular coat. The values obtained from a vessel so different in dimensions from the human brachial could not be applied without qualification to the latter. And even with the ox carotid, differences (apparently due to local causes) as large as those sometimes found in the human limbs were observed only under extremely abnormal conditions; application of these results without qualification to the human vascular system would be wholly unwarrantable.

But these observations refer to normal arteries, and, as has been already stated, the differences in man have been noticed by us only in the presence of abnormal conditions of the arterial system.

In pathological arteries from the legs of old horses we recorded very high degrees of resistance to compression, the resistance depending on the presence of enormously powerful contraction of the thick muscular coat. But the characters of such arteries on palpation are very different from anything we have felt in human limbs, and it is obviously not permissible to assume the presence of any such amounts of contraction in man.

Mode of Closure of Artery under External Pressure.

A good many years ago von Recklinghausen[7] suggested a different form of closure under external pressure in sclerosed arteries as compared with normal ones, the latter being evenly flattened by external pressure and completely occluded (see the figure C), while in the former the walls of the tube become apposed at the middle part, while chinks still remained open at the sides (B). The fact that different kinds of tubes may undergo one or other form of closure is a fact that is very easily demonstrable. This hypothesis has, however, not gained currency as accounting for differences in pressure readings. It does not explain why *all* thick sclerosed arteries do not give different readings as compared with others in the same individual that are relatively normal. And it would not account for the effects of continued compression already described as occurring in some sclerosed arteries while absent in the great majority.



A indicates the circular form of the uncompressed artery; B represents the peculiar form of closure (with chinks at the sides) described in the text; C shows the ordinary form of closure.

There is evidently another factor concerned, and we find reason to believe that muscular contraction constitutes such; that is, that the determination of the peculiar form of closure above referred to depends on an influence exercised by contraction of the muscular coat of a sclerosed artery under certain conditions. Powerful muscular contraction is not at all necessary. An amount of contraction that is soon overcome by external pressure of an extent sufficient to flatten the tube and bring its walls in apposition is able to determine the persistence of chinks at the sides through which the pulse can still be transmitted; a more or less considerable amount of additional external pressure is needed to close the chinks sufficiently to obliterate the pulse.

The occurrence of different pressure readings in different limbs and variations in the amount of such differences at different times are capable of explanation as being due to variations in the contraction present. The effects of continued or repeated compression—reduction of the readings with subsequent recovery, etc.—are similarly explicable as depending on the demonstrated influence of compression in temporarily removing the tonic contraction, which is again restored after a time, with concomitant restoration of the pressure values. The same explanation applies to the facts that local compression tends to equalize the diverse values which may be obtained from different limbs at the first test, and that local compression (even if repeated) does not reduce the reading below the level obtained with a soft artery.

The view here stated differs from that of von Recklinghausen in postulating activity of the arterial muscle as an essential factor, in addition to the presence of certain structural alterations in the sclerosed artery; it differs from that of Russell (who has long urged the importance of hypertonus in normal and sclerosed arteries), inasmuch as the latter seems to regard the muscular resistance as simply opposing flattening, not as determining a special form of closure.

An Illustrative Case.

If the pressure readings from two limbs differ markedly on account of the occurrence of a special form of closure in one artery as compared with the other, the pulse persisting much longer in one than in the other, it might be possible to elicit special evidence bearing upon the different conditions. Such we have sometimes observed definitely; indeed, it was the encountering of certain facts in comparative and simultaneous estimations on different limbs, in some cases giving widely different systolic readings, that led us to regard the above-described mechanism as an operative one; the way in which it harmonized with other facts was sufficiently obvious.

In the following case, examined with Dr. J. R. Murray, these phenomena were very striking. The patient had no aortic regurgitation, but the arm-leg difference in the systolic readings was very marked. At the first test the (simultaneous) obliteration values were 115 for the upper arm and 198 for the leg. But a very marked change was recognizable in the leg artery at 116 mm.—that is, at the obliteration level in the arm. The pulse in the leg, though not abolished, was very notably cut down in volume; it persisted as a pulse of small volume with very little alteration till it became obliterated—at a much higher level.

Repeated compression was tried and was found to give marked lowering in the leg readings at successive tests—

namely, 198, 186, 168, 149, 148 mm. A similar change occurred in the relation of the points of disappearance and reappearance of the pulse in successive observations. At first, when the armlet pressure was raised sufficiently to obliterate the pulse, kept at this level for some time and then lowered, the pulse did not reappear until a very much lower level had been reached—154 mm.—as compared with 198. The armlet pressure, run up again, gave disappearance of the pulse at 182 and reappearance at 152. The armlet pressure was then lowered to zero for some time; the next compression gave disappearance at 186 and reappearance at 155. At a later compression the pulse disappeared at 168 and reappeared at 166. There was thus a progressive diminution of both the actual obliteration level and of the difference between the points of disappearance and reappearance.

The arm readings behaved in a strikingly different way. There was no appreciable difference (a very few millimetres) between the points of disappearance and reappearance of the pulse, and the readings remained steady at about 115 to 116 throughout the series of observations, while the leg readings were showing extensive changes; this indicates that the aortic systolic pressure remained unchanged. It was easy in repeated observations to predicate the arm values by noting the very definite change in volume in the leg artery, as already described.

In this case diastolic pressure estimation by the auditory and oscillatory (Pachon) methods gave similar values—75 to 85 mm.—in arm and leg, varying little at the beginning and end of the series of observations.

It is noteworthy that the systolic readings were much higher with the armlet on the calf of the leg than when on the thigh; the latter often nearly agreed with the arm.

We conclude from such results that the systolic pressure was really the same in the arm and leg, despite the fact that a very much higher armlet pressure was required to obliterate the pulse in the leg, though the latter pulse was strikingly cut down—to one of very small volume, which persisted until the compressing armlet pressure had been raised much higher. We interpret this result as being due to a different form of closure in the arm and leg arteries respectively, and we regard the leg arteries as the ones in which the behaviour of the tube under compression was peculiar. There is, of course, the question as to whether the abnormality is in the arm or the leg—that is, whether complete occlusion is abnormally difficult in the leg or abnormally easy in the arm; either of these would obviously cause a discrepancy in the readings, the intra-arterial pressure being similar in both arm and leg.

There is clear evidence that the abnormality is in the leg. The arm readings remained constant, being unaffected by repeated or continued compression, while the leg readings changed very strikingly, being enormously reduced by repeated or continued compression; the leg readings could thus be brought down towards equality with the arm readings, but showed no further reduction—below the arm value—on further compression. And after a time the leg readings recovered their great predominance over the arm values.

These phenomena fit in exactly with the conception of a peculiar form of closure of the leg arteries when compressed by the "armlet," central parts being brought into apposition a considerable time before the lateral chinks are closed; the pulse continues to be transmitted until a more or less considerable excess of external pressure has been applied, over and above what is needed to stop the transmission of the pulse in a normal artery. The effects of continued or repeated compression in reducing the readings in such an artery find an obvious explanation in their demonstrated influence in reducing the resistance of the arterial wall by temporarily diminishing or annulling the contraction present, and so removing a factor concerned in inducing the peculiar form of closure above described in a sclerosed artery.

Resistance to Compression of Excised Arteries.

In view of the foregoing results, it may be asked whether the high resistance to compression recorded in strongly contracted surviving arteries, possessing thick muscular coats, is associated with a similar peculiarity in the mode of closure under external pressure or whether it is simply due to the direct resistance presented (by the rigid muscle) against distortion of the tube from the circular form.

The excised arteries in which very high resistances were encountered were always powerfully contracted, with rigid muscular coats and a very small lumen. The use of the term "contraction" in this connexion may be ambiguous; it may mean that the action of the (shortened) muscular fibres may be such as to reduce the lumen to very small dimensions; or, on the other hand, the muscle may be "contracted" and rigid while the lumen is not very small—for example, in presence of high internal pressure, under the influence of cold, etc.; in the latter case, the muscle may be firmer and more resistant without being much shortened.

In the case of a strongly contracted artery with a very small lumen, there is no evidence that the peculiar form above described ever occurs in such a way as to allow persistent passage of the pulse wave through lateral chinks. The small lumen seems always to close by a simple apposition of the walls of the tube.

We conclude that the excess of external pressure over internal pressure which is necessary to obliterate the pulse under those conditions is due to the direct resistance to distortion of the rigid muscular walls of the tube. But, as already stated, we find no ground for assuming the existence of anything resembling this degree of muscular rigidity in the vessels of the living subjects. At the same time, the presence of contraction — that is, muscular resistance — is very important in human arteries when associated with certain abnormal structural conditions, determining the occurrence of special features in the process of closure of the vessel by external pressure, and thus leading to different readings of obliteration pressure that do not correspond with differences in the actual systolic pressure.*

REFERENCES.

[1] Hill, Flack, and McQueen, *Proc. Roy. Soc.*, 1914, lxxxvii, 255. [2] Janeway and Park, *Arch. of Intern. Med.*, 1910, vi, 586. [3] MacWilliam, *Proc. Roy. Soc.*, 1902, lxx, 109. [4] MacWilliam and Kesson, *Heart*, 1913, iv, 279. [5] MacWilliam and Melvin, *Heart*. 1914, v, 153; BRITISH MEDICAL JOURNAL, March 28th, 1914. [6] MacWilliam, Melvin, and Murray, *Proc. Physiol. Soc.*, March 14th, 1914. [7] von Recklinghausen, *Arch. f. exper. Pathol. u. Pharmak.*, 1901, xlvi, 104. [8] Russell, *Arterial Hypertonus, Sclerosis, and Blood Pressure*, 1908, 87; BRITISH MEDICAL JOURNAL, 1912, i, 659.

---

* By "closure" is meant such a degree of occlusion as is necessary to stop the transmission of the pulse wave as tested on the peripheral side.

Reprinted from the British Medical Journal, *April 17th, 1915.*

BLOOD PRESSURE ESTIMATION IN CHILDREN.

BY
G. SPENCER MELVIN, M.D.,
LECTURER ON EXPERIMENTAL PHYSIOLOGY,
AND
J. R. MURRAY, M.D.,
SENIOR ASSISTANT IN PHYSIOLOGY, IN THE UNIVERSITY OF ABERDEEN.

It is practically impossible at the present moment to meet with any class of patient or any clinical condition of which no record of blood pressure exists. Till recently it seemed almost impossible to break fresh ground or to supply data that were original and not merely confirmatory or contradictory. But from the present standpoint of sphygmomanometry these existing records must be regarded as vitally incomplete. Blood pressure, clinically interpreted, consists of a more or less constant pressure—the diastolic pressure—on which there is periodically superimposed an additional pressure—the systolic pressure. So long as there was no method of determining the extent of the constant strain on the blood vessels due to the diastolic pressure, "blood pressure readings" was a term synonymous with "systolic pressure readings." There has certainly for some time existed a class of apparatus designed to make good this serious deficiency. While some of these instruments were cumbersome in structure or complicated in the method of working, all suffered from a lack of definition in the indication (maximum oscillation, etc.) they were designed to give. Moreover, the theory on which they were based is one which must now be regarded as interesting but inaccurate.

Application of the Auditory Method in Children.

This method is simple and determinate. By experiment and investigation it has been established as accurate. A doubt in our own minds as to the applicability of the method in the case of the small arteries of children led to our carrying out a series of determinations. We were early satisfied that the phenomena were not only very definite, but were in many cases as definite as those in adults; in fact, the clearest impression of the sounds we have yet obtained was obtained in the case of a child.

The apparatus required for the application of the method in children are:

1. A mercury manometer (preferably an ordinary one). The slight advantage in portability of the compressed-air type of manometer is depreciated by the necessity in its use for frequent calibration to ensure accuracy.
2. An armlet of suitable size, much narrower than the ordinary one for adults; an armlet of 8 cm. broad does very well—for example, that supplied with the Pachon oscillometer.*
3. Some form of filler, either of the "ball" type or of the "screw compressor" type. The latter, greatly superior for finer adjustments of pressure, suffers in having a fixed capacity. This difficulty can, however, be easily overcome.
4. An Oliver tambour with strap attachment, which secures it in a fixed position on the arm. Such an arrangement leaves the observer with both hands free—an important point.
5. Rubber tubing and connexions.

With such an apparatus, extremely simple and portable, it is possible to do a complete blood pressure estimation. In making a determination, the armlet is fitted snugly but not tightly to the upper arm, and the tambour (phonendoscope) is strapped lightly over the site of the brachial artery of the same arm at the bend of the elbow. The strap of the tambour should not constrict the arm, but should be sufficiently tight only to prevent movement of the tambour, which then lies practically without pressure on the skin. With the ear pieces fitting properly in the ears of the observer, both his hands are free. One hand should be utilized to palpate the radial pulse of the arm under investigation, the other to manipulate the compressor. The armlet should now be inflated till the external pressure thus established is considerably higher than that at which the radial pulse was felt to disappear.

It is perhaps desirable in the meantime to proceed with the next step, before directing attention to the significance of the phenomena appreciated. The next step consists in the gradual lowering of the external obliterating pressure. At a certain point, most probably while yet no pulse is appreciable by tactile examination at the wrist, a distinct sound is heard. Careful attention directed to the quality and intensity of this sound will enable the observer to note the following alterations, first proposed by Ettinger, and now pretty generally accepted by workers at the method: The sound at first clear cut, the *first phase* as it is called, develops a murmurish quality—the *second phase*. This, later, is replaced by a clear sound—the *third phase*. The onset of the *fourth phase* is marked by the transformation of this loud, clear sound into a dull sound of less intensity. The complete abolition of the sound is referred to as the *fifth phase*.

Significance of the Phases.

Experiment has shown that attention must be directed to two of these phases:

Phase 1.—The onset of the sharp, clear sound. The external pressure indicated by the manometer at the point at which phase 1—that is, the beginning of sound—represents systolic pressure.

---

* Supplied by Hawksley.

Phase 4.—The commencement of the fourth phase—that is, the point at which the sound, from being loud and clear, becomes dull and diminished in intensity—is an indication of diastolic pressure. By some observers the fifth phase—that is, the point at which the sounds disappear—was regarded as indicating diastolic pressure; but it must be admitted that such a view is untenable.

Table of Results Obtained from Healthy Children.

No.	Age.	Pulse-Rate.	Auditory Systolic.	Auditory Diastolic.	Pulse Pressure.	No.	Age.	Pulse-Rate.	Auditory Systolic.	Auditory Diastolic.	Pulse Pressure.
1	10	100	108	80	28	21	7	128	110	60	50
2	12	102	105	78	27	22	12	128	100	80	20
3	10	60	90	55	35	23	7	100	106	85	21
4	12½	50	108	65	43	24	5	95	114	90	24
5	14	84	108	78	30	25	4	90	102	58	44
6	12	84	115	80	35	26	10	80	106	55	51
7	12	84	113	77	36	27	5	70	95	55	40
8	10	92	110	86	24	28	10	90	110	78	32
9	12	100	110	70	40	29	6	120	120	80	40
10	13	106	100	70	30	30	11	106	108	62	46
11	8	104	112	75	37	31	13	60	90	70	20
12	14	88	106	68	38	32	11	90	120	90	30
13	9	80	108	75	33	33	4	80	90	60	30
14	8	90	120	70	50	34	9	93	120	80	40
15	11	100	120	90	30	35	8	104	115	75	40
16	7	120	110	60	50	36	6	92	106	78	28
17	11	65	120	65	55	37	8	96	100	70	30
18	9	96	90	62	28	38	11	82	120	85	35
19	12	96	120	80	40	39	11	126	130	80	50
20	5	132	90	50	40	40	4½	84	100	70	30

Averages: Age, 9.5; pulse-rate, 93.6; auditory systolic, 108.1; auditory diastolic, 72.4; pulse pressure, 35.7.

For the actual determination of these pressures all that is required is that the observer gradually lower the external obliterating pressure, and note the external pressure corresponding to (*a*) the onset of the sound; (*b*) the onset of thefourth phase. He will then be in possession of the valuesof the systolic and diastolic pressures.

We make it a point to determine that the auditory systolic index exceeds the tactile systolic index—that is, that the first sound is heard at a higher level of external pressure than that at which the pulse is felt to return at the wrist. This is almost invariably the case, and is to be insisted on. Otherwise—that is, if the pulse be felt before the sound is heard—we do not proceed with the estimation, unless, as generally happens, it be possible, by adjustment of the tambour, or other alteration, to establish the proper relation of auditory systolic index at least as high as tactile systolic index.

The extent of pressure to which the sound persists after the diastolic index—that is, the duration of the fourth phase—is very variable in young adults. It seems to depend in part, but by no means wholly, on the degree of quiet prevailing in the surroundings in which the examination is made. In children a fourth phase of any considerable duration is very rarely found.*

The method, as will thus be seen, is exceedingly simple, and to a very large extent removes the personal equation which with other methods often results in appreciably different estimations. From personal experience we gladly welcome a method which, especially in the case of children, substitutes the delicate sense of hearing for the coarser and more variable sense of touch. Its simplicity and ease of application, together with the portability of the apparatus employed, makes its employment possible in almost every conceivable situation.† Above all, it is accurate both as regards systolic and diastolic pressure values, without which properties no method of blood pressure estimation has at the present day any legitimate right to the title.

The tabular statement (p. 133) shows some of the results we have obtained from investigations made on forty children. These children, of ages between 4 and 14 years, had an average age of 9.5 years. So far as we could make out, they were, as far as the circulatory system was concerned, healthy, so that our results are to be taken as applying to normal children. No such data have hitherto been supplied; they are obviously essential as a basis for the study of blood pressure in disease.

Estimated by the auditory method, the average systolic pressure is seen to be 108.1, the average diastolic pressure to be 72.4, and the average pulse pressure 35.7 mm. Hg.

The cardiac output is, of course, very small in children, and in association with this the capillary system to be filled is very limited as compared with the adult. Yet, from our results, it is to be noted that the systolic pressure is only very slightly lower in children than in adults. Various observers, using the much less accurate tactile method, have estimated the average systolic pressure in children at decidedly lower values, for example, 90 mm. mercury. But the fallacies of the tactile index are much more serious in young children than in adults, and the results by the auditory method are so sharp and precise as to admit of no doubt.

---

* The fourth phase rarely amounts to more than 2 to 3 mm. in children—in only one case of the present series was a prolonged phase got (Case No. 8, Table).

† An obvious exception is in noisy surroundings.

The average diastolic level, on the other hand, is decidedly higher in children than in adults; this is the main cause of the considerably smaller pulse pressure in children—35.7 mm.—as compared with 46 mm. in adults.

Comparison of Children and Young Adults.

The relation between the values obtained in a series of fifty-nine healthy young adults and in the present series of children is as follows:

	Adults.	Children.
Systolic pressure ...	... 111.8 ...	108.1
Diastolic pressure	... 65.7 ...	72.4
Pulse pressure ...	... 46.0 ...	35.7

The average pulse-rate in children was 93.6 (range 132–50), and it is noteworthy that, while a slow pulse naturally tends to give a lower diastolic pressure (by allowing longer time for the blood to escape from the arterial system into the capillaries between the beats), the adjustment of the vascular system may be such as to give a diastolic pressure quite up to the normal, in presence even of a markedly slow heart-rate—for example, Cases Nos. 4 and 31 in table.

Some other points of comparison between children and adults may be stated. By the tactile method the average systolic pressure was 105.7 in children as compared with 108.7 in adults, while the range was 125–84 in the former and 132–92 in the latter.

By the auditory method the range of systolic pressure was 130–90 in children and 135–92 in adults, while the range of diastolic pressure was 90–50 in the former as compared with 82–50 in the latter.

In children the relation of pulse pressure to systolic pressure was 1 : 3 and to diastolic pressure 1 : 2, while in adults this relation was 1 : 2.7 and 1 : 1.6 respectively.

The normal readings of systolic and diastolic pressures and of pulse pressures in children, as described above, are so definite and reliable as to constitute a sound basis for the study of pathological variations and their significance.

We have to record our thanks to Professor J. A. MacWilliam for much kind advice and assistance in this investigation.

THIS BOOK IS DUE ON THE LAST DATE
STAMPED BELOW

AN INITIAL FINE OF 25 CENTS
WILL BE ASSESSED FOR FAILURE TO RETURN THIS BOOK ON THE DATE DUE. THE PENALTY WILL INCREASE TO 50 CENTS ON THE FOURTH DAY AND TO $1.00 ON THE SEVENTH DAY OVERDUE.

BIOLOGY LIBRARY

NOV 14 1933

LD 21-5m-7,'33

QP6
P5
BIOLOGY
LIBRARY
G
Physiological
422611